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VOL. 34, NO. 2 AUGUST, 1960

Twenty-fifth Annual Convention
Philadelphia, Pennsylvania
23, 24, 25, 26 October 1960

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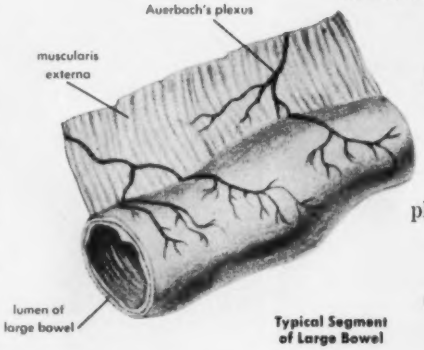

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VOL. 34, No. 2 AUGUST, 1960

THE American Journal OF Gastroenterology

(FORMERLY THE REVIEW OF GASTROENTEROLOGY)

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1. Weiss, J.: Amer. J. Gastroent., July 1960.
2. Breidenbach, L. and Secor, S. M.: Amer. J. Surg., Jan. 1957.

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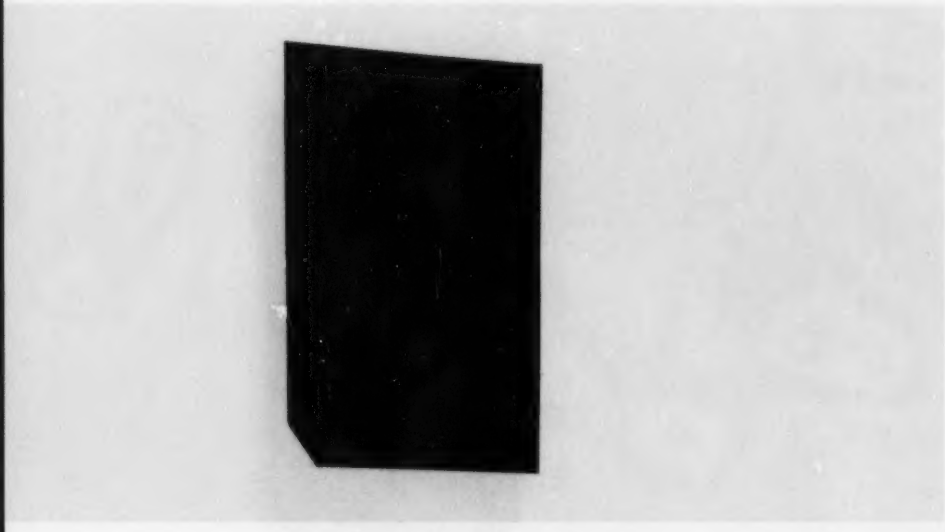

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1. Morgan, L. A., and Parks, R. E., Radiology 74:436, March 1960

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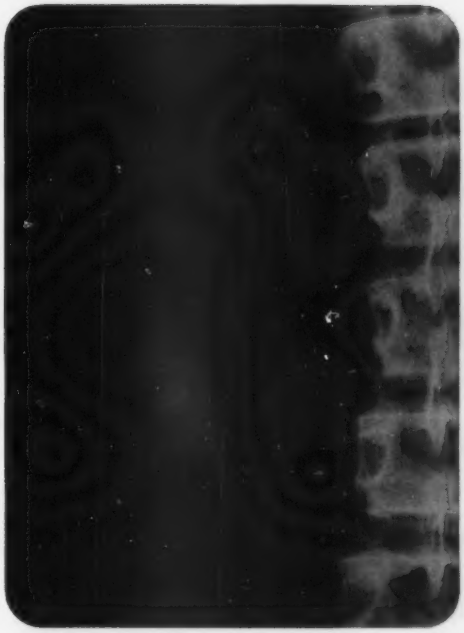

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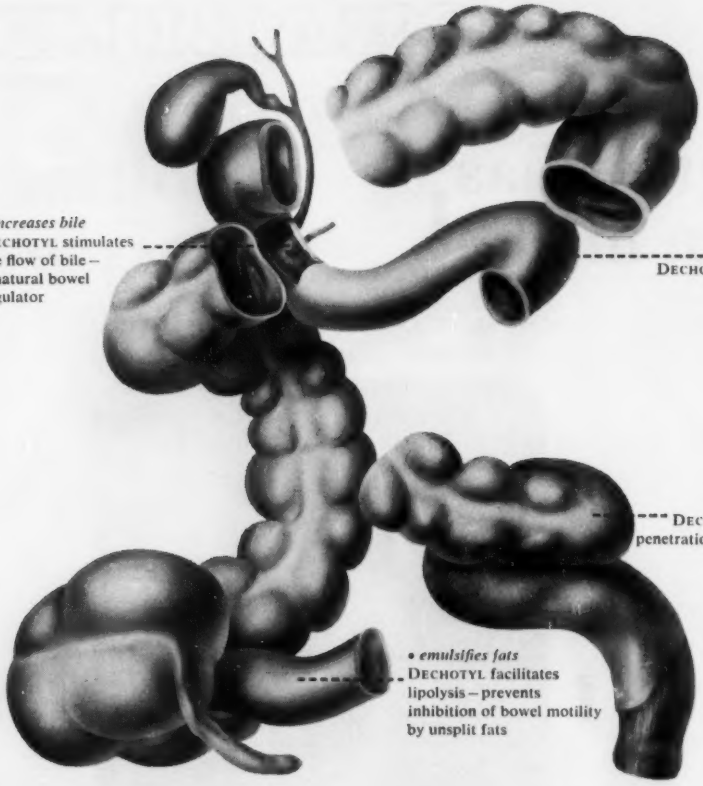

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VOLUME 34 AUGUST, 1960 NUMBER 2

DIAGNOSIS OF INTESTINAL PARASITES*

JOHN KESSEL, Ph.D.

Los Angeles, Calif.

I appreciate this promotion to be the first speaker this morning and shall try first to give you a short review of a few of the more important aspects of the laboratory diagnosis of amebiasis.

To date no satisfactory serologic test for diagnosing amebiasis has been developed. One must, therefore, still rely on the microscopic examination of stools, pus from abscesses or scrapings from intestinal ulcers. This material is examined either for trophozoites or for cysts.

The importance of the second point, namely, the use of the sigmoidoscope and proctoscope in taking scrapings from ulcers, still requires emphasis. You perhaps remember the story about our noted Sir William Osler, who was on ward rounds one day and reviewed a case that was suspected as being amebiasis. The assistant giving the report said that although amebiasis was suspected, the stool report from the laboratory was negative.

Sir William promptly said, "Have you performed a proctoscopic examination?" It had not been done, but upon completion, trophozoites of *Endameba histolytica* were found. Taking scrapings by proctoscopic or sigmoidoscopic examinations are still important, for one often finds a positive by that method which has been negative by stool examination.

The complement-fixation test has been discarded in amebiasis because no satisfactory antigen has been developed. A precipitin test (the Moan test) has been described, but todate no agreement of results has come from different laboratories.

Later I shall speak of Dr. Biddle's skin test, in which she is much interested at present, but before we proceed to that, I should like to remind you

*Presented before the Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Los Angeles, Calif., 24, 25, 26 September 1959.

that examination of the three types of material which I have just mentioned, falls under three main headings.

First, the preliminary examination, either in saline solution, in which one can observe the motility of the actively moving trophozoite; or by applying to a portion of the film a drop of iodine solution. This stains the trophozoites or the cysts and makes it possible to differentiate many immediately.

A certain percentage, however, are not definite, and make necessary the second procedure, i.e. examination of permanently stained films. These films are usually fixed in Schaudinn's fluid and stained either with Heindenhain's iron hematoxylin which is the old favorite and gives the best detail for study of cytology; or with the trichrome stain which has been accepted by the California State Department of Public Health for routine laboratory work. It has the advantage of being more quickly and easily performed and does not stain the nuclei or other structures as perfectly as the iron hematoxylin stain, but for a permanent record, it is suitable.

The third procedure is concentration of a small portion of stool for cysts by the zinc sulfate or other approved method. The first lantern slide will show a composite of a series of examinations by the different methods.

You will notice that if six stool examinations are made by the preliminary saline iodine film, only about 50 per cent of infections are detected. If one uses both preliminary saline and iodine films and zinc sulfate concentration, the percentage of positives detected increases to 70 or 80 per cent. If one uses all three methods, the results are much superior and one will detect from 90 to 95 per cent of the positive cases.

[Slide] Slide two shows the results of 5,678 stool examinations at the Los Angeles County Hospital between 1929 and 1932.

Several points of special interest may be noted. First, the individuals examined in this series all exhibited some gastrointestinal or hepatic disturbance. Among these, only 3.2 per cent were found to be positive for *E. histolytica*. I remember in those days certain surveys were reporting 10 or 20 per cent positive among the general population. Here, however, one observes that stools from the average hospital patient suspected of having gastrointestinal symptoms yielded a lower rate than usually suspected. Many were from patients with bacterial infections which were positive by culture. These tended to lower the over all protozoal prevalence.

A second point of interest is the comparison of results this year (1959) with 30 years ago. One often hears the statement, "Amebiasis is over with. One finds only low percentages of positive stools in hospital examinations". In this same stool diagnostic laboratory today, at the Los Angeles County Hospital, 2 per cent of the stools are positive for *E. histolytica*, a reduction of about one-third.

I have checked the results within the last few months in three hospitals in Los Angeles and each showed from 2 to 3 per cent of patients to be positive for *E. histolytica*. Amebiasis is, therefore, still with us as a clinical problem.

I will say, however, that I think improved sanitation, better treatment, which Dr. Wharton and many others have been using throughout the country, should have a profound effect in reducing the percentage of positives.

It is also often thought that the common use of antibiotics has an effect in reducing amebic infections.

You will notice in Table I of 181 people positive for *E. histolytica*, that 21 per cent showed an acute amebic dysentery, 60 per cent fell under the heading

TABLE I

THE LOS ANGELES COUNTY GENERAL HOSPITAL LABORATORY FINDINGS

Number of patients examined for *E. histolytica*	5678
Number of patients positive for *E. histolytica*	181
Percentage of patients positive for *E. histolytica*	3.2
Percentage of positive patients showing acute amebic dysentery	21.0
Percentage of positive patients showing chronic colitis symptoms	60.0
Percentage of positive patients showing no subjective symptoms	19.0
Percentage of positive patients showing amebic liver abscess	10.0

of chronic amebiasis and 19 per cent fell under the heading of carriers, sometimes called "cyst passers".

Another point of interest is that in 1932 about 10 per cent of those positive for *E. histolytica* were individuals with hepatic symptoms, most of them with a definite liver abscess. Today earlier recognition of amebiasis has led to fewer hepatic findings.

[Slide] The next slide will show a group of individuals who applied for positions as food handlers in 1940. You will notice that 5 per cent showed *E. histolytica* in their stools. *Shigella flexneri* was also found in 5 per cent of the stools.

During the last year, 100 prospective food handlers examined at the Los Angeles County Hospital showed only 2 per cent positive for *E. histolytica* and

1 per cent positive for Shigella. These results, likewise, reflect the benefit of improved sanitation.

I shall present Dr. Biddle's phase of the work.

Dr. Biddle, who is Microbiologist at the Los Angeles County Hospital and Professor of Parasitology at the School of Medicine, University of Southern California, has been studying the development of a skin test for amebiasis. She and Dr. Wharton encountered a liver abscess from which a large amount of pus was procured. This was frozen and subsequently used as an antigen.

In this study two antigen controls were developed, one from a culture of *E. histolytica* and the other of liver cells from a normal individual. These were tested on negative rabbits and guinea pigs, which were likewise negative for *E. histolytica*.

Then these three antigens were tested on a series of some 70 individuals, eight of whom at the time were experiencing liver symptomatology or intestinal amebiasis. Diagnosis has been confirmed by finding *E. histolytica* either in the liver abscess pus or in the stool.

Of that series, all eight were positive by this skin test. The skin test reaction is of two types. The immediate reaction [slide], in which one sees a wheal just above the top of the ruler. This is probably two or three centimeters in diameter comparing it with previous photographs. This immediate reaction appears within 30 minutes.

Of these eight positive individuals, six showed immediate reaction; two out of the eight demonstrated the delayed type of reaction and one out of the eight had both.

In the series, apparently there were five with liver symptomatology. Four of the five had immediate reaction, one delayed, and one showed both types.

This test is provocative and suggests that Dr. Biddle may have an antigen that will aid in diagnosis. It indicates, if one can combine the amebic antigen with the tissue substance, that superior antigenicity occurs. Perhaps that interaction between *E. histolytica* and tissue is necessary in order to provide a suitable antigen. This may explain why so many serologic tests that have been tried down through the years have not met with any degree of success, because the amebic antigen produced in a culture tube was an incomplete antigen. May we wish Dr. Biddle success with this study.

May I review briefly some recent ideas on species and strains of *E. histolytica*. I attended the International Congress of Tropical Medicine in Lisbon just about a year ago, where a symposium on amebiasis was held. First, the commonly accepted view in the United States is to treat *E. histolytica* whenever

found in stools. This applies not only to the large race but to the small race as well.

In Europe quite a different opinion exists. They conclude that only strains coming from tropical areas are of any significance. The individuals who have never been out of France or England, who show *E. histolytica*, seldom, if ever, exhibit symptoms and, therefore, harbor strains which are not pathogenic. "It is not necessary to treat such persons".

This idea was first proposed by Brumpt in 1924, who harbored for some 16 years a strain which morphologically was *Endameba histolytica*. Because of lack of symptoms, he named it *Endameba dispar*. In his experiments, *E. dispar* produced less pathology in kittens than strains from acute amebiasis.

In 1912, Prowazek proposed the name *Endameba hartmanni* for a small ameba of man. For many years most workers considered this only a small race of *E. histolytica*. Now the name *E. hartmanni* has been revived to designate a small ameba, nonpathogenic for man which produces cysts less than 10 microns in diameter.

Several workers have tested the pathogenicity of various strains of amebas in animals. For many years, the accepted work on this subject was that of Meleney and Frye in this country, in which they used a series of kittens. They found certain very definite strain variations which, according to their system, showed pathogenic indices ranging from 0.3 to 1.9. Most large race strains from acute amebic dysentery produced a high pathogenic index in kittens. They found, likewise, a strain with a high index recovered from a carrier, thereby indicating that a carrier may be a potential danger and should be treated.

The one small race ameba that they tested showed a pathogenic index of 0.3 which was very low.

Neal has used rats instead of kittens and he finds a high percentage of correlation between severity of symptoms in man and rats when testing large race strains. A strain from a carrier, however, produced severe symptoms in rats. Amebas recovered from people who had never been out of England, usually showed a low pathogenicity for rats. Small races of *E. histolytica* likewise produced little pathogenicity in rats. If these findings are confirmed, one might conclude that: 1. a tropical climate has an effect either on the parasite or the host in inducing acute symptoms and 2. small race *E. histolytica* at times designated as *E. hartmanni* produces less severe pathology in experimental animals than large race *E. histolytica*.

It will be interesting to know what the experiences have been of members of this society concerning cases of amebiasis. Do all cases of acute amebic dysentery originate in the tropics or do some of them originate in our own country?

TREATMENT OF ALIMENTARY WORM INFESTATIONS*

JAMES N. DE LAMATER, M.D.

Pasadena, Calif.

It is unfortunately as true today, as it was centuries ago, that the prevalence of helminthic infections in man is due to his inability to insulate himself against his own excretions. In those areas where sanitation has developed to a high degree, diseases caused by worms show a markedly reduced incidence. They are prevalent in areas where ignorance and squalor persist. It has been estimated, that among a world population in excess of 2,500 million people, there are many more than this number of helminthic infestations. These figures alone indicate the area in which eradication will be most effective. But it may take years, if not generations, in some areas, for education and engineering to come in contact with the individual.

It was not many years ago that malaria seemed an insoluble problem. And to those of us who had some measure of responsibility for its control in the second war, the reduction of this disease was a most rewarding experience. Malaria control is not only a matter of education, it is a matter also of sanitation, engineering, and chemistry. It is doubtless true that with what is already known of the parasite, the vectors, and geography of this disease, it could be wiped out in any area once the economic necessity presented itself.

Human infestations by worms are in much the same position. Some life cycles of the parasites have been understood for centuries, others for shorter periods, but most for long enough and with sufficient understanding so that once approached in a given environment, with sufficient determination, there would be no reason for their ultimate survival.

The first approach to helminthic diseases then, demands attention to their prevention.

Treatment of alimentary worm infestations has benefited largely by recent pharmacologic advances—new chemical agents are now available which are more effective against the worm and in reduced toxicity upon the host. Individual treatment has thus been made less obnoxious and more efficient.

Of the 30 or so helminthic diseases, there are relatively few I wish to discuss today, as follows:

Nematohelminthes – Class Nematoda

1. Hookworm — *Necator americanus*
   Ancylstoma duodenali

*Presented before the Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Los Angeles, Calif., 24, 25, 26 September 1959.

2. Strongyloidiasis *Strongyloides stercoralis*
3. Ascariasis *Ascaris lumbricoides*
4. Trichuriasis *Trichuris trichuria*
5. Enterobiasis *Enterobius vermicularis*
6. Trichinosis *Trichinella spiralis*

Platyhelminthes

a) Class Trematoda
Schistosomiasis, etc.

These worms will not be considered.

b) Class Cestoda

1. Diphyllobothriasis *Diphyllobothrium latum*
2. Taeniasis Saginata *Taenia saginata*
3. Taeniasis Solium *Taenia solium*
4. Hymenolepiasis *Hymenolepis nana*
5. Dipylidiasis *Dipylidium caninum*

NEMATODES

Hookworm disease:—Supportive measures directed to the anemia and nutrition should be considered simultaneously with any specific therapy against the worms. In cases of average severity, attention to anemia and diet can be made after treatment with antihelminthic agents. In cases with severe anemia appropriate supportive measures must be instituted first including transfusion in seriously ill patients.

The current choice of drugs is tetrachlorethylene, though hexylresorcinol, carbon tetrachloride and oil of chenopodium are useful under some circumstances.

Tetrachlorethylene, in gelatin capsules, is given in doses of 3.0 c.c. for adults; 0.2 c.c. for each year of life for children, in one dose. The night before treatment the diet is restricted to a light, fat free, meal; and the morning of treatment no breakfast is allowed. After medication, a saline cathartic of sodium sulfate, 30 gm., in water is administered. No food is allowed for at least 4 hours and no alcohol for 24 hours.

If ascariasis is also present, it must be treated first, as tetrachlorethylene may cause migration of this worm with serious consequences. In this case, pipe-

razine salts, hexylresorcinol or Hetrazan can be used. Hexylresorcinol used in treating concurrent hookworm and ascaris may be entirely adequate for both infestations.

Carbon tetrachloride and oil of chenopodium are more toxic and, if anything, less effective but because of reduced cost can be used on a large scale basis which makes the other agents economically impractical.

Strongyloidiasis:—In this threadworm infestation, dithiazamine (Delvex) has recently been reported as very effective, given as 200 mg. enteric coated tablets t.i.d. for 21 days. Repeated stool examinations should be made following completion of treatment to evaluate results. Gentian violet is also an effective agent. It is usually given in enteric coated capsules designed to release the drug about one hour after ingestion. In doses of 65 mg. t.i.d. for 16 days for adults, the dose for children is reduced according to size and age. Treatment failures are common, requiring repeated exhibitions of the drug.

Ascariasis:—This is one of the more common worms in this area.

Only symptomatic treatment can be used during the period of pulmonary involvement by migrating larvae.

Ascaris lumbricoides is readily expelled from the intestine after therapy with piperazine salts which have low toxicity, are easy to administer and are effective. Piperazine is given in doses of .5 to 1.0 gm. of piperazine hexahydrate t.i.d. for 7 days. Single doses up to 3.0 gm. have also been used in adults. No dietary precautions are needed and no before or after purgation indicated. Piperazine citrate (antipar) or phosphate (antipate) and other commercial preparations marketed as syrups are available.

Removal of adult worms can also be accomplished safely with hexylresorcinol in hard gelatin capsules. The dose for adults is 1 gm.; for children 0.1 gm. for each year of age. Treatment can be repeated every 4 to 5 days if necessary.

More recently terramycin and aureomycin have been found effective in eliminating ascaris in cats, and recent trials show them to be effective also in man.

Hetrazan, introduced as a filaricide, is also an effective low toxicity compound which may be given in doses of 6 mg. per pound of body weight, daily, for four days. Two or three courses of treatment at 3-4 week intervals may be needed.

Trichuriasis:—The whip worm is a very difficult worm to remove because of its location, partially buried in the wall of the cecum or colon.

Recently introduced (Delvex) dithiazamine is at present the most effective trichiuricide. The recommended dose is 20 mg. per pound of body weight, divided in three daily doses, with a maximum of 200 mg. daily for 5 days. The

drug may cause mild vomiting and diarrhea but no more serious toxicity has as yet been reported.

Hexylresorcinol is not highly efficient but is readily available. It is given in doses of 1 gm. for adults: .1 gm. per year of age for children and is followed in 3 hours with a saline purge. No food is allowed for 6 to 8 hours after medication. The procedure may have to be repeated frequently at four or five-day intervals.

When involvement of the colon is extensive, 0.1 per cent aqueous hexylresorcinol enemas may be given, care being taken by means of petrolatum to protect the buttocks from burns.

Terramycin has not been shown to be as effective as in enterobius infestations but in a disease as resistant as trichuriasis, it deserves a therapeutic trial in usual doses.

Enterobiasis:—Pin worm infestations are considered as group infections, as the eggs are easily transmitted to members of a family or other close living groups.

The piperazine salts [citrate (antipar) and phosphate (antipate)] are very effective. The following dosages according to the patient's weight are recommended for a period of seven days.

Weight	*Equivalent Piperazine Hexahydrate*
Up to 15 pounds	0.25 gm.
16 - 30 pounds	0.5 gm.
31 - 60 pounds	1.0 gm.
Over 60 pounds	2.0 gm.

Vanquin, a cyamine dye, has likewise been found to be very effective and is given in doses of .6 to .7 mg. per kilogram of body weight, three times daily for 5 or 6 days. Mild gastrointestinal symptoms may occur but do not require withdrawal of the drug.

Hygienic measures are imperative; hand washing and adequate laundering of personal and bed clothing are essential in preventing spread of the ova.

Those who have wrestled with the mess caused by gentian violet can utter a prayer of thanks that something better has at last been found.

Cestodes

The tapeworms: Diphyllobothrium latum, Taenia solium, Taenia saginata, Hymenolepis nana, Hymenolepis dimunta and *Dipylidium caninum* are the spe-

cies of tapeworm most commonly found in man. Of these, *T. saginata* and *H. nana* are the most common.

Quinacrine hydrochloride (atabrine) is effective in all forms, but appropriate preparation of the patient is essential if treatment failures are to be avoided.

The day before treatment, the patient is placed on a liquid diet, and that evening a saline cathartic given. The morning of treatment the patient receives a cleansing enema and while still fasting, atabrine is administered in a 1 gm. dose. One to 2 hours later a second saline purge is given and all stool specimens are searched for the scolex. If the scolex is not recovered, stools are reexamined in three or four weeks and if proglottids and eggs are present, retreatment is recommended.

Antibiotics, phenothiazines and cyamine dyes effective in other helminth infections are not effective with tapeworms.

The last several years have brought much progress in the treatment of these diseases. The next several will bring more and when properly integrated with sanitation, engineering and education may well contribute to the eradication of this enormous group of infestations.

AMEBIC LIVER ABSCESS RUPTURED INTO THE DIGESTIVE TUBE*

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Mexico, D. F.

Amebiasis is quite common in the human race. The infestation figures vary within wide limits in different countries and in the various parts of the same country.

According to Beltrán, from 15 to 34 per cent of the adult population of Mexico is infested with *Endameba histolytica*. Flores-López, of Mexico City General Hospital, reports amebiasis in 25 to 40 per cent of the patients of the Gastroenterology Unit. In 1,000 consecutive patients seen at the Hospital for Nutritional Diseases, Mexico City, Gual and de la Vega found 338 cases (33.8 per cent).

The most common clinical manifestation of amebiasis is, of course, dysentery. This syndrome occurred in 153 of 3,000 cases of intestinal amebiasis in Peña and Ruiloba's series of patients admitted to the last mentioned hospital between 1946 and 1952. This represents an incidence of 5.1 per cent. But the attack of the parasite is not always confined to the intestine. Sometimes it goes on against other organs, primarily the liver. This happened in 43 instances in Peña and Ruiloba's series (1.4 per cent).

Dr. Costero, former Chief Pathologist at the Mexico City General Hospital, says: ". . . the general opinion is that in every case of active intestinal amebiasis there is a hepatitis of variable degree which, due to the considerable resistance of the liver against the parasite, does not show up by either clinical or laboratory methods".

The production of an amebic hepatic abscess is due to the lytic activity of the parasite's enzymes and also to vascular thrombosis with resulting necrosis of the liver substance.

Fournier, summarizing a paper of Dr. Miguel Jiménez written in 1856, says: ". . . the wall of the abscess varies according to the duration of the disease. In every case it is irregular in shape. In early cases one gets the impression that several isolated cavities have communicated to make a bigger one. A young abscess has the following features, described from within outside: 1. the characteristic chocolate-colored pus; 2. a thicker, but unorganized layer; 3. tissue rags attached to the wall; 4. purulent softening of the parenchyma; 5. inflamed glandular tissue, and 6. surrounding healthy liver substance." When an abscess becomes secondarily infected it contains, in addition, several bacterial strains, mainly *B. coli*, *B. paracoli*, *Streptococcus faecalis* and *Clostridia*.

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Rupture of an amebic liver abscess into the neighboring structures is a very serious complication, which entails great mortality. Much of our present knowledge regarding hepatic amebiasis is due to Dr. Miguel Jiménez, a famous 19th Century Mexican physician, whose earlier report on the subject before the Academia Nacional de Medicina was published 117 years ago, in 1842. Ten years later, he reported 297 cases of amebic hepatic abscess. Of this number, 34 ruptured into various organs.

Perforation occurred then, as at present, mainly into the bronchi and the pleural cavity. Six out of 34 perforations occurred into the digestive tube: one into the stomach and five into the colon.

In 1956 the Gastroenterology Unit of the General Hospital reported 30 cases of ruptured amebic liver abscess, with only one instance of perforation into the digestive tube (colon) (Haro y Paz). This patient died, as did 13 more of the complicated cases.

From Ward #29 of the same hospital come two reports: one case of amebic hepatic abscess opened into the first part of the duodenum (Haddad), and another of an abscess opened at three sites: the upper third of the greater curvature of the stomach, the general peritoneal cavity and the pericordial sac (Jiménez, Elías).

As far as necropsy material data is concerned, the latest information available is that of Flores-Barroeta, Núñez and Biagi from the Department of Pathology, School of Medicine, National University of Mexico. In April, 1959, they reported their findings in 2,203 autopsies performed between 1954 and 1958.

One hundred and nine cases of hepatic abscess were found—an incidence of almost 5 per cent. In 98 of the 109 cases of hepatic abscess, amebiasis was found to be directly or indirectly the cause of death. Ninety-two of the 109 cases of hepatic abscess were of amebic nature.

The right lobe of the liver was involved in 85 per cent of the 92 cases. In 36 per cent of these right-sided abscesses other amebic lesions were found somewhere else in the liver.

The contention that the amebic hepatic abscess is single is, once more, disproved. More than two abscesses were found in over half of the cases.

Of the 92 autopsy cases of amebic hepatic abscess, 56 were complicated (60 per cent). The most frequent complication was rupture into the peritoneal cavity; this happened in 28 instances, or one-half of the perforated cases. It will be noted that in clinical material the most common site of rupture is into the bronchi and pleural cavity.

Finally, rupture into the digestive tube occurred in the following nine cases: twice into the stomach, five times into the duodenum, and twice into the colon.

Two personal cases of amebic abscess of the liver ruptured into the digestive tube are presented.

In the first one, the writer was called in consultation to see a man, 27 years old, who had been 5 weeks in treatment for supposed typhoid fever. The correct diagnosis proved to be amebic abscess of the liver with perforations to: 1. the hepatic flexure of the colon, 2. the superior genu of the duodenum, and, later 3. externally through the abdominal wall in the right upper quadrant, with establishment of a duodenal fistula and a colonic fistula. These complications led to the death of the patient in spite of specific, though protracted, antiamebic treatment and supportive measures.

The second case was that of a man of 54 who gradually developed fever, chills, intractable nausea, epigastric and right subcostal pain, mild yellow discoloration of the teguments, severe loss of weight (17 kilos) and the feeling of a mass in the right upper abdominal quadrant. He went on for 6 weeks with practically no treatment. Two diagnostic possibilities were contemplated: 1. amebic abscess of the liver, and 2. malignancy. A barium meal revealed a large extragastric mass (liver) greatly displacing the stomach and duodenum, and prompt passing of the contrast medium into the liver substance, where some gas images could also be seen. The roentgenologist was unable to say whether the perforation occurred into the first part of the duodenum or into the gastric antrum. Antiamebic, antibiotic and supportive measures were put in practice and the patient made a dramatic recovery in a matter of a few days.

Summary and Conclusions

1. From 15 to 40 per cent of the adult population of Mexico is infested with *Endameba histolytica*.

2. The most common clinical manifestation of amebiasis is dysentery. It occurs in about 5 per cent of the infested persons.

3. Hepatic amebiasis occurs in 1.4 per cent of the cases of intestinal amebiasis.

4. Anybody infested with *Endameba histolytica* is a potential candidate to develop a hepatic amebic abscess.

5. Rupture of an amebic hepatic abscess into neighboring structures is a serious complication. It happens in neglected, untreated or maltreated cases.

6. An amebic hepatic abscess can, and will, open into the digestive tube. Several clinical and autopsy cases collected from the Mexican medical literature are mentioned.

7. Two personal cases are added. In the first one, the abscess opened into the duodenum, the hepatic flexure of the colon, and externally through the

abdominal wall. This patient died. In the second case, the abscess ruptured either into the stomach or into the duodenum, in the vicinity of the pylorus. The x-ray films show the passing of the contrast medium, during the gastroduodenal examination, into the liver substance, where some gas images can also be seen. The patient made a dramatic recovery in a few days of medical treatment (emetine chlorhydrate, tetracycline, chloroquine and supportive measures).

Discussion

Dr. George K. Wharton:—I did not come prepared to act as Moderator. I will, however, do my best.

We have to expect an increasing amount of acute infection from the various parasites, especially amebas, with the increase in means of travel and the number of people who travel.

We are faced with a problem in this city, and probably over this country, because of the poor results possible from stool examinations done by accepted laboratory technics. I have been very disappointed in the results. Maybe they are right; maybe I am expecting too many cases to be positive.

There is excessive expense in running the number of stools that should be done and in going through the various steps that Dr. Kessel mentioned.

It is too soon to give you any more than some of the findings of the skin test that Dr. Biddle and I have been developing. I do not intend to interpret them now. In all the cases of large race amebiasis, however, we have had positive skin tests. In the cases of liver abscess, Dr. Kessel has given the figures. In patients who have had amebiasis, who may be relatively symptom-free, we have found about 50 per cent with positive skin tests but negative stools. Does this mean that the skin tests are too sensitive, or does it mean that with some treatment amebiasis clears from the gastrointestinal tract and is hard to find?

In six cases of amebiasis, which had adequate treatment, skin tests returned to negative within two months.

I would like Dr. Kessel or Dr. DeLamater to comment on the relationship between previous infection of amebiasis and the development of chronic ulcerative colitis. Two papers that were given at the World Congress of Gastroenterology a year and a half ago mentioned that bacillary dysentery increased the tendency to the development of ulcerative lesions in the colon.

I realize that there are many questions that have not been answered this morning, nor probably can they be answered this morning. There is one that has been asked of Dr. DeLamater: "What symptoms make you suspect ascariasis, especially if an original infestation has passed?"

Dr. DeLamater:—There are no typical symptoms of ascariasis, and one establishes the diagnosis only upon doing stool examinations.

There may, however, be vague abdominal symptoms: loss of appetite, cramping abdominal distress, but nothing particularly which points a finger at this disease. There are situations, of course, in which the migration of the worm may result in acute specific symptoms as when it invades or destroys the bowel.

Some medications irritate these worms and cause migration. I saw a woman about a year and a half ago who had been taking something—I never was able really to determine what—and she had a worm crawl out of her nose one morning while she was taking a bath. Such episodes, of course, make the diagnosis evident, but usually one arrives at the diagnosis only upon finding either the worms or the eggs in the stool.

I would like to say just a word about the predisposition of ulcerative colitis, let's say, to amebiasis or Flexner infections. In this part of the world certainly the incidence of ulcerative colitis is quite irrelevant to the incidence of amebiasis. Indeed, I have never seen complicating amebiasis in an established case of ulcerative colitis, although I am sure that it exists. It has been reported in the literature that bacillary dysenteries, have from time to time been a precipitating mechanism of ulcerative colitis. This may well be, but I think it has been shown without question that ulcerative colitis occurs in certain types of immature individuals, and that it is most probably of psychogenic origin. It is certainly possible that an episode of acute bacillary dysentery could be a precipitating factor, but beyond this I think there is no evidence that ulcerative colitis *per se* is a sequel to either of these two diseases.

ALCOHOL METABOLISM IN HEPATIC DYSFUNCTION

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Inasmuch as the liver is the primary site of the metabolism of alcohol, the latter has been studied as a possible aid in the evaluation of hepatic function. Clinical studies of this type were first reported in Europe, in 1938, using oral ingestion of alcohol and measuring blood alcohol levels. European investigators have reported a reasonably good correlation between liver disease and a delayed fall in blood alcohol levels[1-6]. A similar approach has been used in this study, using a modified Harger Drunkometer for breath analysis for the estimation of blood alcohol levels.

Normal Metabolism of Alcohol

To evaluate alcohol metabolism in hepatic dysfunction, it is first necessary to describe the physiology involved. This can be divided into absorption, dispersion, and finally, oxidation of alcohol. The first phase, absorption, is simple, as alcohol is very rapidly absorbed, even through the stomach, without alteration. This has been demonstrated in fasting dogs, in which over half the alcohol ingested was absorbed in 15 minutes and practically all of it within 1-2 hours[7]. Although a high concentration of alcohol can greatly delay absorption, it does not appear to be a problem in this study[8].

The dispersion of alcohol following absorption occurs quickly, as all organs and fluids of the body contain alcohol within a few minutes after ingestion. Equilibrium between blood and muscle alcohol in animals has been found to occur within 10 to 30 minutes after intravenous injection of alcohol, while this balance is somewhat delayed for the whole body[9,10]. The dispersion of alcohol can be computed and measured as the ratio of alcohol concentration in the whole body to blood alcohol (Widmark factor "r"). This varies from 0.52 to 0.67 and is not always constant for the same individual. Tissue analysis of alcohol has demonstrated a constant ratio, unaffected by blood alcohol concentration, and amounting to an average of 0.60 in the liver, 0.15 in fat, near absence in bone, and 0.75 in remaining tissues[10]. A tendency for elevation of factor "r" in thin individuals, the male sex and in the presence of fever would be expected to

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reflect lower blood alcohol levels; therefore, recognition of these conditions possibly should be considered when evaluating alcohol metabolism in liver disease[10,11].

The final phase of alcohol metabolism involves its oxidation. The first step requires an enzyme, alcohol dehydrogenase of the liver, which oxidizes alcohol to acetaldehyde. The formation of acetaldehyde requires DPN (diphosphopyridine nucleotide), an enzyme which is also essential in the metabolism of pyruvate, acetate and glucose[12]. In many tissues the acetaldehyde is then readily oxidized or converted to other products, many of which enter the tricarboxylic acid cycle[13]. The rate of oxidation of alcohol is unaffected by exercise, normally being 10 to 20 mg. per cent per hour[10]. This is called Widmark factor "β", which may vary in different individuals, as well as from hour to hour in the same subject, due to unknown factors. The amount of alcohol oxidized per hour is obtained by multiplying "β" x "r" x body weight, which is equivalent to about 20 ml. of whiskey in the 70 kg. man[7].

The rate of catabolism of alcohol may be affected by many factors other than liver disease, chief of which are dietary. Ingestion of food accelerates oxidation of alcohol, with amino acids being more potent than fatty acids[11-14]. Similarly, measuring either blood alcohol or metabolism of alcohol in liver slices, alanine and pyruvate increased the rate of catabolism. Clinical studies measuring peak alcohol blood levels and studies on rat liver homogenates, indicate that the type of diet recently ingested may also affect alcohol oxidation[6-15]. A normal diet afforded optimal catabolism, followed by a high protein diet, carbohydrate and finally a high fat diet. In the rat studies a protein-free diet depressed alcohol oxidation to a greater extent than starvation or 50 per cent restriction of diet. Other factors which may affect the blood alcohol level include the size of the liver and a history of previous alcohol consumption. Studies in cats suggest a lower rate of oxidation in larger animals, perhaps because of a tendency to have a relatively smaller liver[11]. The problem of tolerance was also studied in cats, in which alcohol had been added to milk. There was no change in oxidation rate because of hepatic enlargement, but there was a decrease when based on unit weight of liver[11]. This may explain the normal values of liver tests in some patients with hepatomegaly. Zieve and Hill, in their study of influence of alcohol consumption on hepatic function in healthy, gainfully employed men, postulated that the better than average liver tests may be due to existence of hyperfunctioning cells, resulting from minimal damage[16].

Recent studies of zinc metabolism in cirrhosis of the liver have increased the knowledge of alcohol metabolism in liver disease[17]. Zinc has been found to play an indispensable role in carboxypeptidase activity and several dehydrogenases, which include alcohol dehydrogenase and glutamic dehyrogenase of the liver. In severe postalcoholic cirrhosis the zinc content in the serum and liver was found to be low, while the urinary output of zinc was high. The liver

TABLE I

NORMAL LIVER: GROUP I PATIENTS

Case	Age	Sex	BSP	Alcohol level mg.%	Other liver tests	Diet	Alcohol intake	Physical abnormalities	Miscellaneous
1	40	F	0	20,18	Normal	Fair	Little	None	Formerly heavy alcohol intake
2	54	F	0	20	"	Poor	"	"	
3	40	F	0.9	0	"	Fair	"	"	
4	52	M	1	18	"	"	"	"	Severe emphysema
5	58	M	1	7	"	"	Moderate	"	
7	60	M	1.3	12	"	Good	"	"	Diabetic
8	43	F	1.58	4	"	Fair	Little	"	
9	42	F	1.7	35	"	"	"	"	
10	59	M	2	5	"	Normal	"	Huge abd. mass	Diagnosis: not known
11	82	M	2	7	"	"	Moderate	Normal	
12	50	M	2	16,19	Glob. 3.8	Fair	Heavy	"	Diabetes
14	33	F	2.5	0	Normal	Good	None	"	
15	40	M	2.8	2	"	"	"	"	
17	39	F	3	0,0	"	"	Little	"	
19	60	M	3	17	"	Poor	"	"	
20	55	F	3	4	"	"	None	"	Diabetes
21	42	M	3	0	"	Fair	Moderate	Pleural effusion	
22	50	M	3	0	"	"	Heavy	Normal	
23	60	M	3.3	11	"	Good	Little	"	
24	68	M	3.6	0	"	Fair	Moderate	"	
25	46	F	3.6	21,18	"	Poor	None	"	
26	72	M	3.8	2	"	Fair	Heavy	Liver 2 cm.	
27	76	M	3.9	13	"	"	Moderate	Normal	Formerly heavy alcohol intake
28	60	M	4	16	"	Poor	Little	Very obese	
29	62	F	4	16	"	"	"	Liver 2 cm.	
30	70	M	4	5	"	Fair	"	Normal	
31	69	M	4.4	11	"	Good	"	"	

29	62	F	4	16	"	"	"	Liver 2 cm.	
30	70	M	4	5	"	Fair	"	Normal	
31	69	M	4.4	11	"	Good	"	"	
32	30	M	4.4	12,15	"	"	"	"	Occasional borderline elevation of bilirubin
33	23	M	4.5	1	"	Fair	Moderate	"	
34	50	M	4.9	4	"	"	Little	Obese	
36	39	F	4.9	0	"	Poor	"	Normal	
37	30	F	5	5	"	Normal	"	"	

TABLE II

BORDERLINE LIVER ABNORMALITY: GROUP II PATIENTS

Case	Age	Sex	BSP	Alcohol level mg.%	Other liver tests	Diet	Alcohol intake	Physical abnormalities	Miscellaneous
16	25	M	2.8	16	Bil. 2.5-1	Good	Little	None	Constitutional hepatic dysfunction?
35	36	F	4.9	9	Glob. 4.0 Ceph. floc. 3,3	Fair "	"	Liver 3 cm.	Mild heart failure
38	72	M	5.3	0	Glob. 3.75	"	"	None	
39	57	M	5.5	9	Normal	"	Moderate	"	
40	39	M	5.6	9	"	"	Little	"	Recent pneumonia
42	65	F	6	9	"	"	"	"	Sphincterotomy 2 mos. ago
44	65	M	6	7,3	"	"	"	"	
45	71	F	7.3	0	"	"	"	"	
46	74	M	8	44,34	"	Poor	None	"	
47	40	M	8.1	21	"	Fair	Moderate	"	
48	50	F	8.6	16,18	"	Good	Little	Obese	Diabetic
49	32	F	9	22	"	"	"	None	Hepatitis 3 mos. before

disease was considered to cause a "conditioned deficiency" of zinc in which normal intake failed to meet the needs of the organism, perhaps related to the increased urinary excretion. Possibly, the deficiency could also be derived from inadequate intake in the diet. By giving zinc sulfate in capsules in physiological amounts, the zincuria disappeared except in the most severe cases; and in several patients the bromsulfalein retention improved. The decreased zinc concentration in the liver could not be established as coming from the hepatic parenchyma, however, as fibrosis could cause a similar finding. Depletion of zinc in the above metalloenzymes probably does occur, however, as based on other findings. For example, the deficiency of zinc in a mold caused its complete loss of alcohol dehydrogenase activity and diminished its protein synthesis. The liver alcohol dehydrogenase, however, differs from the pure yeast alcohol dehydrogenase: the former can oxidize other alcohols, among which are glycerol and Vitamin A; it can lose its capacity to metabolize or to survive in the presence of high concentration of alcohol; and finally, it is much less potent than the yeast enzyme. Liver alcohol dehydrogenase affects several other metabolic pathways, such as protein anabolism, so that interference with this enzyme could have many serious effects. Studies on horse liver alcohol dehydrogenase, an enzyme similar to the human, revealed an increasing activity up to a peak of 90 mg. per cent blood alcohol level. This decreased to 50 per cent of its peak activity when the blood alcohol was 0.46 gm. per cent equivalent to the amount found in a severely intoxicated person.

Method

Ninety-five per cent ethyl alcohol was given to 74 subjects of the inpatient and outpatient services of the Indianapolis General Hospital in a dosage of 0.5 gm./kg. of body weight. The chilled drink diluted to a 25 per cent solution either with water or fruit juice was ingested by the fasting individual within 15 minutes, although an extension to one hour probably would not have affected the results. Since 1 gm. of 95 per cent alcohol equals 1.25 ml., the dosage for a 70 kg. subject would be equivalent to 3 fl. oz. of 100 proof whiskey. Three- and 4-hour blood alcohol levels, checked twice, were obtained by using a modified Harger Drunkometer to determine alcohol in the expired air. The 3-hour level was obtained primarily as a check on the procedure, as the rate of descent of blood alcohol is fairly constant. Liver function tests included 45-minute bromsulfalein, bilirubin, thymol turbidity, cephalin flocculation, serum proteins and alkaline phosphatase tests. Four-hour blood alcohol levels of 0-10 mg. per cent were considered normal, 10.1-20 mg. per cent, borderline, and above 20 mg. per cent, abnormal.

A complete description of the analysis of alcohol using rebreathed air is given by Harger[18]. Alveolar air is obtained by exhaling deeply into a collapsed, warm, polyethylene, 2-quart frozen food bag, and then rebreathing this air four times. An incubator is used to maintain the temperature of the bag and exhaled

air at approximately 28° C for the prevention of condensation. Since the milligrams of alcohol in 1 ml. of blood is equivalent to the amount of alcohol in 2,100 ml. of alveolar air, a simple formula can be used to calculate the blood alcohol. By this method it becomes unnecessary to analyze the breath sample for CO_2, as is now done in the standard Drunkometer procedure. The end point is reached when 0.169 mg. of alcohol is passed through the reagent consisting of sulphuric acid and potassium permanganate. When the blood alcohol concentration is low, several liters of rebreathed air are needed to reach this point. This is remedied by using one-fifth as much permanganate and changing the two color standards*. Titration with a known alcohol solution has shown that the micro Drunkometer method is accurate.

Results

The 74 subjects were numbered in sequence according to degree of bromsulfalein retention and have been recorded in three tables, representing normal liver, 32 cases; borderline liver abnormality, 12 cases; and liver disease, 30 cases. Patients having a 45-minute bromsulfalein retention above 10 mg. per cent were classified as having liver disease, while levels 5.1-10 mg. per cent were considered to be borderline, unless there were other indications of liver disease. Other liver tests and physical abnormalities were listed only when abnormal, while the dietary and alcohol intake were recorded only as gross impressions.

Evaluating the alcohol test in relation to the status of liver function is difficult with the information available. In the absence of a better test, reliance often had to be placed on the unrepeated bromsulfalein test alone for classification of the subjects. Its limitations must be realized since significant dye retention may be demonstrated from many nonspecific causes[19]. Also, the bromsulfalein and other liver tests may occasionally be normal suggesting good functional capacity, yet the patient may have proven liver disease[20].

The results of the alcohol tolerance test in the three groups of patients have been summarized in Table IV for simplification. Unexpected results occurred at a minimum in group I (normal liver) and group II (borderline liver abnormality), being 3 and 8 per cent, respectively. Because of the nature of cases of group II, it is difficult to ascertain what represents an unexpected result. For this reason, only the markedly delayed alcohol metabolism of Case 46 was considered in this category. Possibly some significance may be attached to the fact that 2 of the 4 patients having had abnormal results in group I and II had had hepatitis within 8 months prior to the test. A history of poor diet or heavy alcohol intake may also affect alcohol metabolism. In the normal liver group, this history was obtained from 17 per cent of patients having a normal test, compared to 50 per cent in those having a borderline alcohol test.

*a.—2 ml. 5% $CoSO_4$ plus 13 ml. of water.
b.—1 ml. 5% $CoSO_4$ plus 18 ml. of water plus 1 ml. of 0.19 $K_2Cr_2O_7$.

TABLE III

LIVER DISEASE: GROUP III PATIENTS

Case	Age	Sex	BSP	Alcohol level mg.%	Other liver tests	Diet	Alcohol intake	Physical abnormalities	Miscellaneous
6	58	F	1.1	8,8	Normal	Fair	Light	Liver 10 cm.	Biopsy: Mild triaditis
13	58	F	2	21	"	"	Moderate	Liver 7cm.firm	
18	46	M	3	18	"	Poor	Heavy	Liver 5cm.firm	
41	57	F	5.9	8	"	Fair	None	Liver 5cm.firm	
43	68	F	6.8	24,21	"	"	"	Liver 5 cm.	
50	50	M	10.1	93	Not done	Poor	Heavy	Liver 4cm.firm	
51	76	M	10.2	25	Normal	Fair	Moderate	Normal	
52	65	F	10.4	19	Ceph. floc. 3,3	Poor	Light	Liver 5 cm.	
53	63	F	10.7	2,3	Ceph. floc. 4,4 Thy. Turb. 8	Fair	"	Liver 4 cm. Spleen 4 cm.	Biopsy: chronic triaditis
54	75	M	13	5	Alb. 2.61	"	Heavy	Liver 5cm.firm	
55	68	M	13	27	Alk. phos. 15	"	Moderate	Normal	
56	60	M	14.7	2,1	Normal	Good	"	Liver 3 cm.	Lymphatic leukemia
57	50	F	14.9	54	Ceph. floc. 3,3	Fair	"	Liver 2 cm. Spider nevi	Previous hematemesis Esoph. varices
58	63	F	15	17	Alk. ph: 15 KA	"	Light	Liver 10 cm.	Recent heart failure
59	38	F	15.1	38	Ceph. floc. 3,3	"	"	Cruvelheir Baum. Syndrome	Hepatic coma 1 yr. ago
60	56	F	15.5	8,60,11	Normal	"	None		Mild hyperthyroidism
61	51	F	17.4	6,7	All abnormal except Alb.	"	Moderate	Liver 9 cm.	

60	56	F	15.5	8,60,11	Normal	"	None		Mild hyperthyroidism
61	51	F	17.4	6,7	All abnormal except Alb.	"	Moderate	Liver 9 cm.	
62	49	M	21.2	27	Ceph. floc. 3,3	"	"	Liver & Spleen 4 cm.	
63	55	F	22	30	Normal	"	Light	Liver 5 cm.	Lymphoma
64	75	M	25	28	"	"	Heavy	Liver 5 cm.	
65	61	F	27	2,3	Thy. Turb. 8	"	Light	Liver 5 cm.	
66	51	M	27	44	Alb. 2.7 Ceph. floc. 3,4 Bil. 1.25	Poor	Heavy		Severe cirrhotic Died 2 mos. later Prolonged heart failure
67	45	M	27.4	9	Glob. 4	Fair	Light	Liver 8 cm.	
68	49	M	28.1	14	Normal	"	Heavy	Liver 4 cm.	
69	47	M	35	39,1	Ceph. floc. 4,4 Bil. 4, Thy. T. 9; Glob. 4		"	Liver 3 cm.	Severe cirrhosis improved
70	63	M	43.4	75	Glob. 4.3, Ceph. floc. 3,4 Bil. 1.4		Heavy	Hard, nodular liver; ascites	
71	60	M	49.7	45	Ceph. floc. 3,4		"	Liver 4 cm.	
72	60	M	52	42	Alb. 2.2, Glob. 3.8; Bil. 3.4 Alk. phos. 15		"	Ascites, edema	
73	48	M		35	Alk. phos. 23 Ceph. floc. 3,3 Bil. 20.6		"	Ascites; Nodular liver	
74	44	M		30	Bil. 3.8; Alb. 2.5; Ceph. floc. 3,3; Glob. 4.9 Thy. Turb. 18		"	Ascites	Died in two weeks

In group III patients, in whom all were considered to have liver dysfunction, 27 per cent had normal alcohol tests and 16 per cent had borderline tests. Factors to consider in explaining these results include the dietary or alcoholic history, liver size, heterogeneity of cases selected, and finally the frequency of other liver tests being normal.

Resembling group I patients, a history of dietary deficiency or alcohol excess in group III occurred much more frequently in those patients having delayed alcohol catabolism than in those having normal liver alcohol tests. Fifty to 60 per cent of both the borderline and abnormal alcohol test patients gave this history compared to 13 per cent (one) of the eight patients having normal alcohol tests.

TABLE IV

SUMMARY OF RESULTS OF THE ALCOHOL TOLERANCE TEST

Group	Total Cases	Alcohol Tests: number and per cent of total		
		Normal	Borderline abnormal	Abnormal
I. Normal liver	32	18 (56%)	13 (41%)	1* (3%)
II. Boderline liver abnormality	12	7 (60%)	2 (15%)	3** (25%)
III. Liver disease	30	8 (27%)	5 (16%)	17 (57%)

*Patient had an attack of hepatitis 8 months previously; biopsy at present is normal.
**One patient had an attack of hepatitis 3 months previously.

Liver size may be a factor in alcohol metabolism, as all of the patients of group III having normal alcohol tests had hepatomegaly as compared to 65 per cent of those having abnormal alcohol tests.

The heterogeneity of group III patients has been mentioned because the incidence of diseases secondarily affecting liver function appears much higher in those patients having normal or borderline alcohol tests. Of the eight having normal alcohol metabolism, two had "triaditis" of undetermined etiology, one leukemia, and another congestive heart failure†. The latter diagnosis and hyperthyroidism were diagnosed in two of the five patients having borderline alcohol tests. On the other hand, the etiology of the liver disease in 16 of the 17 patients having abnormal alcohol tests was considered as either hepatitis or cirrhosis.

Finally, it may also be stated that other liver tests in group III were not infrequently normal. For example, the bromsulfalein test was essentially normal

†The triads showed a mild to moderate increase in inflammatory cells without apparent increase in connective tissue.

in four patients. Normal tests irrespective of the bromsulfalein test occurred in 38 per cent of patients having normal alcohol tests, 40 per cent having borderline abnormal tests, and 29 per cent having abnormal alcohol tests.

In summarizing the 3 tables no definite conclusions can be made, except perhaps, that false positive tests rarely occurred. A history of recent hepatitis, poor nutrition, and liver enlargement may be significant factors to consider when evaluating alcohol metabolism in itself or regarding liver function. Finally, a greater delay in oxidation of alcohol was usually found in the more severe cirrhotics, but there were some exceptions.

Comment

Alcohol metabolism in liver disease has been evaluated by several methods. One of the first measured the effect on alcohol metabolism when portions of the liver were removed from experimental animals. Abnormal results occurred when 20 per cent of the liver was removed, while other liver tests required at least 70-80 per cent removal[21]. Alcohol tolerance tests similar to the one discussed in this paper have been evaluated by several investigators[1-6]. Liver disease was found to cause a delay in oxidation of alcohol as measured by the 4-hour blood level, but did not affect the peak concentration. The results of Bernstein and Staub were similar to the present study in that 10 per cent of 32 normal subjects had an abnormal 4-hour blood level[5]. For their patients with liver disease, however, 32 cases of diffuse parenchymatous involvement were used, and only 13 per cent gave values below 20 mg. per cent. Obstructive jaundice could not be distinguished from diffuse liver damage. They concluded that the test could qualitatively detect liver damage, but not quantitatively, since there was considerable overlapping of results in patients with different degrees of liver damage. Similar alcohol tolerance tests have also demonstrated that liver disease can minimize the effect of recent ingestion of food on alcohol metabolism. The normal individual, on the other hand, will have a smaller peak and will show a more rapid catabolism of alcohol when he has not fasted[3]. Alcohol tolerance tests also suggest that a recent attack of hepatitis may cause a continued delay of metabolism of alcohol even though several months have elapsed and other tests are normal. This was previously described in one case and possibly explains the discrepancy found in cases 9 and 49[6].

In the final analysis, the rebreathing technic appears to be a satisfactory method for studying alcohol metabolism in hepatic dysfunction. It represents a simple and cheap test requiring no venopunctures, and gives the result within five minutes after the breath sample is collected. Also it is a reproducible test, as shown by the close results obtained in the repeat determinations in 12 of the 13 subjects evaluated; the remaining patient, Case 60, had one confusing and unexplainable result as compared to the initial and final tests. The main objections to the test include the ingestion of a rather strong alcoholic mixture by the

fasting individual, the attitude of certain individuals toward the use of any alcohol, and the slight giddiness noted after ingestion. The peak blood alcohol level seldom exceeds 100 mg. per cent, thereby being within the National Safety Council's "Questionable Influence" range of 50-150 mg. per cent[7]. By taking the previously prepared alcoholic mixture at home, untoward effects are minimized and usually absent by the time he arrives at the laboratory for his 4-hour determination. Finally, the objections listed above may limit its clinical application as a liver function test.

Summary and Conclusions

Alcohol metabolism in hepatic dysfunction was discussed by incorporating results of alcohol tolerance tests and recent studies of zinc metabolism in its relationship to alcohol dehydrogenase. Delayed oxidation of alcohol, zincuria and low hepatic zinc appear to be the main changes in alcohol metabolism in liver disease.

The alcohol tolerance test using the rebreathing technic proved to be a simple and reproducible test, but will have to be studied more carefully in cases with tissue study and other tests of liver function before its efficacy as a liver function test can be determined. Possible variables in the test were discussed under the section of normal metabolism of alcohol. If used as a liver function test it would tend to supplement the bromsulfalein test, and would seem to be most valuable in those circumstances where the latter result may be inaccurate, or of questionable significance.

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THE HEMAGGLUTINATION REACTION FOR VIRAL HEPATITIS IN THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE

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The differential diagnosis of jaundice remains a difficult and often uncertain problem in a significant number of patients. Previous reports by the authors[1-4] have described a hemagglutination phenomenon noted in viral hepatitis. This reaction has been confirmed by Rubin, Kemp and Bennett[5], Havens[6], and McCollum, et al[7]. The phenomenon is noted in both infectious and homologous serum hepatitis. This report describes further experience with this hemagglutination reaction in 40 cases of proven nonviral obstructive jaundice.

A previous report by Morrison and Hoyt[2] described 21 adult patients with proven obstructive nonviral jaundice in whom the hemagglutination reaction for viral hepatitis was consistently negative in 100 per cent of cases tested. In a recent study Havens[6] and McCollum[7] confirmed the authors' experience, reporting negative hemagglutination reactions in all of 23 patients proven to have the obstructive form of jaundice, which included extrahepatic sources of biliary and cholestatic types of jaundice. The hemagglutination technic is currently utilized in the diagnosis and study of various infectious diseases such as influenza and infectious mononucleosis. The method of the authors employs erythrocytes of the macacus rhesus monkey against the serum of patients with viral hepatitis.

Method

Macacus rhesus monkey red blood cells were collected in A.C.D. solution and stored in the refrigerator. A working suspension was prepared by washing the cells 3 times in 0.9 per cent NaCl solution, resuspending them after the last washing to make up a 1 per cent suspension by volume. The working suspension is made up just before using, and unused portions are discarded. The cells

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stored in A.C.D. solution gradually lose their sensitivity and should not be used after 10 days' storage. Two-fold serial dilutions of the patient's serum in 0.2 ml. volume were made in plastic disposable trays to which were added equal volumes of the 1 per cent suspension of red blood cells obtained from macacus rhesus monkey. The serum dilution was incubated for one hour at 37° C. The trays were shaken gently to dislodge the button of sedimented erythrocytes and cells were examined by transmitted light for the presence of clumping. In a negative test the cells can be suspended by gentle agitation into a smooth, homogenous suspension. A positive reaction is indicated by the presence of large to small clumps of cells in the fluid medium. In cases of doubtful positive reactions, it was found that repeating the reading within 20 to 30 minutes will often eliminate false or doubtful positive reactions. The end point was considered to be the highest dilution of serum in which a definite agglutination was macroscopically visible. The conventional scoring was used in the readings and is described below.

4+ the cells are welded into one solid mass

3+ several large irregular clumps with numerous smaller aggregates

2+ moderately large clumps, uniform in size

1+ a granular appearance due to the presence of small clumps of cells

± there is a very finely granular appearance, due to the presence of minute clumps of cells. This is read in comparison with the cell control.

In testing a series of 125 healthy blood donors, it was originally found that 110 had titers of less than 1:8, whereas 13 of 18 persons diagnosed as having an acute attack or recent episode of viral hepatitis, infectious or homologous serum varieties, had titers of 1:8 or greater. These observations had led us to fix the value of 1:8 as the titer which separates normal from elevated readings.

Clinical Material

The blood sera of 38 adults, all jaundiced, were studied. These patients had been hospitalized in various Los Angeles hospitals or were under the medical or laboratory care of the authors. Each was proven to be one of obstructive jaundice by autopsy, laparotomy and/or liver biopsy. These cases consisted of metastatic carcinoma of the liver, choledocholithiasis, cholelithiasis with cholecystitis, cholestatic biliary cirrhosis of the liver, postoperative stricture of the common bile duct, carcinoma of the pancreas, carcinoma of the biliary tract, or obstructive hyperplasia of the sphincter of Oddi. There was one case of carbon tetrachloride poisoning. Sera from nine jaundiced infants were also studied through the courtesy of Dr. Saul Krugman, of Bellevue Hospital, Division of New York University.

Results

It is seen from the foregoing data that of the total of 38 jaundiced cases of adult obstructive, nonviral hepatitis, all (100 per cent) gave negative hemagglutination reactions as reported by the authors[1-4] and independently by Haven[6] and McCollum and associates[7] in smaller groups of patients. Of the nine cases of jaundice tested in infants, however, two cases gave positive reactions, and these two infants were found to have congenital atresia of the bile ducts at autopsy, i.e.: cases of extrahepatic obstructive jaundice. These results indicate false positive hemagglutination reactions in two of nine infants. The difference between adults and infants in reactivity of the phenomena studied in hemagglutinating reactions is not clear at present. Differences in the technics of the hemagglutinating reaction, but not in the results obtained, have been reported by other investigators[6-9]. These differences are mainly concerned with preferences of chick erythrocytes over macacus rhesus erythrocytes to initiate the hemagglutination phenomenon in viral hepatitis. No differences were found, however, in obstructive, nonviral types of jaundice by the use of either chick or macacus rhesus erythrocytes in the hemagglutinating reactions observed by us or by these other investigators[6,7].

Comment

These observations extend our previous findings of a hemagglutination reaction for the macacus rhesus red blood cell associated with virus hepatitis. The mechanism of hemagglutination has not been determined but may be one of three possible ones. Agglutination may result from the direct action of the virus upon the red blood cells, from the action of antibodies formed against the virus which shares immunologic characteristics with the rhesus cells, or from the presence of some abnormal constituent formed in the course of the disease and which has the fortuitous ability to agglutinate the test cells. Regardless of the mechanism involved in the hemagglutination phenomenon, the possibility that obstructive jaundice can be differentiated from viral hepatitis may prove to be of significant clinical value. Instances of fruitless exploratory surgery in jaundiced patients where some mechanical obstructive type of jaundice is suspected preoperatively and viral hepatitis is found at operation are too familiar to require comment.

Since 100 per cent of adult patients in our series of obstructive jaundice as well as each case in Havens' series[6] and McCollum's series[7] failed to show any hemagglutination to viral hepatitis, a negative test in a jaundiced patient should introduce the diagnostic possibility of either obstructive or other form of nonviral hepatitis. On the other hand, a positive hemagglutination test in titers of 1:8 or higher would indicate the probability of viral hepatitis. In patients with considerably elevated titers in ranges of 1:64 and above, the probability of the existence of viral hepatitis may approach certainty. As already

noted, the two infants with obstructive jaundice due to autopsy-proven congenital atresia of the bile ducts gave positive hemagglutination tests. The reason for this anomaly is not clear although various possibilities exist.

Summary and Conclusion

1. The hemagglutination reaction for viral hepatitis was studied in a series of 38 adult cases with proven nonviral obstructive jaundice. The reaction was found to be negative in each of the 38 cases.

2. The hemagglutination reaction was studied in a series of newborn jaundiced patients. It was positive in two cases of congenital atresia of the bile ducts. The reaction was thus inconsistent in two of nine infant cases studied. The cause for this discrepancy in infants is not apparent at present.

3. The hemagglutination phenomenon may be found to be of clinical value in the differential diagnosis of obstructive jaundice in adults.

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SINGLE LARGE NONPARASITIC HEPATIC CYST

Case Report

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The occurrence of a single large nonparasitic hepatic cyst is uncommon in the experience of the individual surgeon. A case is presented herein, and the subject discussed. The surgical therapy utilized was selected in view of the restriction forbidding blood transfusion placed by the anemic patient because of her religious beliefs.

A 67-year old Negro female housekeeper was admitted to The Mountainside Hospital, Montclair, N. J., 1 July 1959, for evaluation of fullness of her abdomen, of five months' duration.

Five months before admission she had an episode of cramps and abdominal pain. She thought her womb had fallen. The cramps abated as soon as she had a bowel motion. She then noted an abdominal mass, but did not seek medical care for several months. Past history was not remarkable, but for a long-standing hypertension. No jaundice or weight loss had been noted.

Physical examination revealed a blood pressure of 200/100. A 14 cm. mobile, nontender mass was found in the upper abdomen. There was no other abnormality. Hemogram showed 3.84 million erythrocytes. Urinalysis, prothrombin time, serum proteins, cephalin flocculation were normal. Intravenous pyelography, confirmed by retrograde studies showed some hydronephrosis on the right with narrowing of the ureter at the mid third. An upper abdominal mass was seen on both the right and left during stages of the retrograde studies. Cholecystogram was normal. Upper gastrointestinal series revealed the antrum stretched over the mass, now on the right side.

A diagnosis of omental or mesenteric cyst was made, because of the relative asymptomatic state of the patient and also the mobility of the mass, both clinically and by x-ray. Abdominal exploration was advised, recognizing the restriction placed by the patient because of her negative attitude towards transfusion.

Abdominal exploration was performed on 8 July 1959, with particular attention being paid to hemostasis. A 19 cm. mobile, thin-walled grey cystic mass, originating from the inferior aspect of the left hepatic lobe was noted. No other intraabdominal variation was found. Pathological consultation at the operating table confirmed the impression of the author that this was a single nonparasitic cyst. Recognizing the anemia of the patient, and the impossibility of transfusion, it was determined to resect all of the cyst but for a 1 cm. cuff attached to the liver. This was easily done, thus avoiding any problem with the many hepatic

blood vessels associated with the cyst at its 7 cm. in length attachment to the liver. The narrow cyst cuff was effectively closed with a locking atraumatic 0 chromic catgut suture, insuring good hemostasis and obliterating the cavity resulting from resection of the cyst. The wound was closed in layers without drainage. The patient recovered swiftly, and was discharged from the hospital in ten days. She is well at this writing, without symptoms or signs of the cyst.

The cyst wall was about 1 mm. thick, and measured 14 x 9 cm. The external surface was dull and marked by plexes of vessels. The smooth inner surface was irregularly trabeculated. Sections show this wall to be composed of a single row of cuboidal cells resting on a layer of relatively acellular collagenous connective tissue, beyond which is a very thin layer of compressed liver tissue. There is a thin fibrous capsule invested by flattened mesothelial cells on the outside.

Comment

Solitary hepatic cysts occur at all ages, but most have been found in patients in the fourth to fifth decades. The etiology is not certain. The various types of epithelium in solitary cysts and the occasional association with inflammatory processes may indicate a multiplicity of causes. Congenital aberrant bile ducts or blood vessels, obstruction of a bile duct by injury or inflammation, neoplastic changes of epithelial tissue, or localized changes secondary to hemorrhage or degeneration have been implicated[1]. Females are more affected. The right lobe is usually involved. The cyst fluid varies from bile colored to clear, with a specific gravity between 1.010 and 1.022[2].

The clinical manifestations of solitary nonparasitic hepatic cysts are like those of benign liver tumors. Pain, the presence of a mass, and symptoms produced by pressure on an adjacent viscera may be noted. The pain may be dull as a result of the size and weight of the tumor, or sharp due to rupture of the cyst or internal hemorrhage.

Laboratory examinations seldom are abnormal. Radiographic studies may show only distortion and displacement of adjacent viscera by the cyst. Torsion, rupture, and infection of the cyst have occurred as complications, producing signs of peritoneal irritation. The diagnosis is difficult before surgery, and many cysts are found at autopsy, having been unknown of in life.

Therapy has varied widely. Aspiration, drainage, marsupialization, resection in part with suture obliteration of the cavity have been done. In addition complete resection of the cyst or anastamosis to the intestinal tract has been performed. Surgical therapy has been effective in most cases in eliminating the mass and symptoms caused by it.

Conclusion

A case of solitary hepatic cyst is presented. Since the experience of any individual with this problem is limited, some discussion of the subject is offered. The surgical attack in this case was selected in order to avoid the need for transfusion in an anemic individual, whose religious beliefs forbade receiving blood.

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CONTROL OF NOCTURNAL SECRETION OF GASTRIC JUICE WITH A LONG-RELEASE DOSAGE FORM OF HEXOCYCLIUM METHYLSULFATE

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Hyperacidity is almost always associated with peptic ulcer. Reduction of hyperacidity is of prime importance for successful medical management and cure of peptic ulcer. Daytime lowering of gastric acidity has not been difficult to maintain. During the waking hours the ingestion of anticholinergic drugs to suppress gastric secretion, and the frequent use of alkalis as well as food to buffer the acid which is secreted, constitute a therapeutic regime which is simple to follow out. During the sleeping hours of the night, however, when total secretion and free hydrochloric acid are at their maximum, management be-

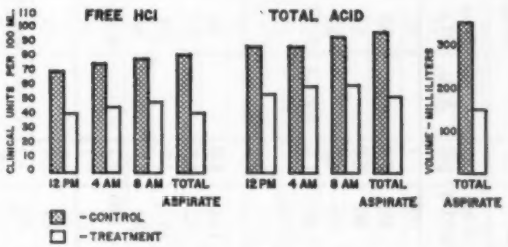

Fig. 1—Free hydrochloric acid, total acid, and volume from continuous aspiration.

comes rather difficult. Levine, Kirsner and Palmer[1] reported that the excessive nighttime secretion of gastric juices, especially of free hydrochloric acid, is an important factor in the delayed healing of certain cases of duodenal ulcer. They found that normal individuals secrete roughly one-half the volume and acidity of ulcer patients. Unless the patient is awakened at frequent intervals to continue the daytime routine, gastric juice of high acid content accumulates and

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TABLE I

Continuous Aspiration

(All Values Expressed in Clinical Units Per 100 Ml.)

				Control				75 mg. hexocyclium long-release				Difference				Comments
Patient	Sex	Age	Time	Vol.	Free HCl.	Total acidity	pH	Vol.	Free HCl.	Total acidity	pH	Vol.	Free HCl.	Total acidity	pH	
S.P. (Duodenal ulcer)	M	44	12:00 p.m.		52	88	2.2		30	42	3.9		−22	−46	+1.7	Excellent reduction of A.S.I. No side-effects
			4:00 a.m.		44	66	2.3		34	39	3.9		−10	−27	+1.6	
			8:00 a.m.		78	89	1.9		31	40	3.9		−47	−49	+2.0	
			Total sample	768 ml.	82	90	1.9	200 ml.	32	40	3.9	−568 ml.	−50	−50	+2.0	
					A.S.I. = 630				A.S.I. = 64				A.S.I. = −90%			
C.R. (Duodenal ulcer)	M	37	12:00 p.m.		125	142	1.6		87	104	1.7		−38	−38	+0.1	Good reduction of A.S.I. No side-effects
			4:00 a.m.		112	122	1.7		54	85	2.2		−58	−37	+0.5	
			8:00 a.m.		110	120	1.7		94	100	1.8		−16	−20	+0.1	
			Total sample	330 ml.	115	130	1.7	200 ml.	60	85	2.0	−130 ml.	−55	−45	+0.3	
					A.S.I. = 380				A.S.I. = 120				A.S.I. = −68%			
T.F. (Duodenal ulcer)	M	34	12:00 p.m.		38	45	3.8		13	20	4.0		−25	−25	+0.2	Excellent reduction of A.S.I. No side-effects
			4:00 a.m.		29	39	3.9	No measurable volume					−29	−39		
			8:00 a.m.		42	54	3.8		7	12	4.1		−35	−42	+0.3	
			Total sample	300 ml.	40	50	3.8	85 ml.	10	23	4.0	−215 ml.	−30	−27	+0.2	
					A.S.I. = 120				A.S.I. = 8.5				A.S.I. = −96%			
M.K. (Duodenal ulcer and ulcerative colitis)	F	57	12:00 p.m.		124	154	1.6		52	94	2.2		−72	−60	+0.6	Good reduction of A.S.I. No side-effects
			4:00 a.m.		130	140	1.5		100	132	1.7		−30	−8	+0.2	
			8:00 a.m.		120	130	1.6		82	98	1.8		−38	−32	+0.2	
			Total sample	450 ml.	122	134	1.6	200 ml.	90	100	1.8	−250 ml.	−32	−34	+0.2	
					A.S.I. = 550				A.S.I. = 180				A.S.I. = −67%			
J.B. (Duodenal	M	67	12:00 p.m.		102	121	1.8		114	130	1.6		+12	+9	−0.2	Poor reduction of A.S.I.
			4:00 a.m.		98	114	1.9		112	125	1.6		+14	+11	−0.3	

colitis)					A.S.I. = 550				A.S.I. = 180				A.S.I. = −67%		
J.B.	M	67	12:00 p.m.		102	121	1.8		114	130	1.6		+12	+9	−0.2
(Duodenal			4:00 a.m.		98	114	1.9		112	125	1.6		+14	+11	−0.3
ulcer)			8:00 a.m.		110	130	1.7		100	126	1.7		−10	−4	0.0
			Total sample	600 ml.	116	132	1.8	500 ml.	112	124	1.7	−100 ml.	−4	−8	−0.1
					A.S.I. = 696				A.S.I. = 560				A.S.I. = −20%		
H.G.	M	71	12:00 p.m.		87	100	1.8			(No measur-			−87	−100	
(Duodenal			4:00 a.m.		70	85	2.0			able volume)			−70	−85	
ulcer)			8:00 a.m.		84	115	1.8		25	47	4.1		−59	−68	+2.3
			Total sample	125 ml.	77	96	1.9	35 ml.	30	41	4.0	−90 ml.	−47	−55	+2.1
					A.S.I. = 96				A.S.I. = 10.5				A.S.I. = −89%		
M.E.	M	42	12:00 p.m.		23	35	4.1		12	20	4.2		−11	−15	+0.1
(Duodenal			4:00 a.m.		20	25	4.1		10	15	4.2		−10	−10	+0.1
ulcer)			8:00 a.m.		22	30	4.1	No meas	urable	volume			−22	−30	
(Prior			Total sample	135 ml.	23	30	4.1	50 ml.	13	20	4.2	−85 ml.	−10	−10	+0.1
therapy)					A.S.I. = 31				A.S.I. = 6.5				A.S.I. = −79%		
T.V.	M	39	12:00 p.m.		32	40	3.9		15	22	4.0		−17	−18	+0.1
(Duodenal			4:00 a.m.		115	125	1.7		12	20	4.1		−103	−105	+1.4
ulcer)			8:00 a.m.		100	112	1.7	No meas	urable	volume			−100	−112	
			Total sample	300 ml.	110	122	1.7	80 ml.	15	28	4.1	−220 ml.	−95	−94	+2.4
					A.S.I. = 330				A.S.I. = 12				A.S.I. = −96%		
J.G.	M	60	12:00 p.m.		48	62	2.5		12	18	4.1		−36	−44	+1.6
(Duodenal			4:00 a.m.		60	75	2.4		22	30	3.9		−38	−45	+1.5
ulcer)			8:00 a.m.		50	60	2.4		25	37	3.9		−25	−23	+1.5
			Total sample	330 ml.	55	80	2.4	85 ml.	23	30	3.9	−245 ml.	−32	−50	+1.5
					A.S.I. = 182				A.S.I. = 19.5				A.S.I. = −89%		
B.K.	M	29	12:00 p.m.		87	100	1.8	No meas	urable	volume			−87	−100	
(Duodenal			4:00 a.m.		74	90	1.9		25	37	4.0		−49	−53	+2.1
ulcer)			8:00 a.m.		75	94	1.9		18	27	4.2		−57	−67	+2.2
			Total sample	225 ml.	85	104	1.8	60 ml.	30	40	3.9	−165 ml.	−55	−64	+2.1
					A.S.I. = 191				A.S.I. = 18				A.S.I. = −91%		

Poor reduction of A.S.I. No side-effects				
Excellent reduction of A.S.I. Slight dryness of mouth				
Excellent reduction of A.S.I. No side-effects				
Excellent reduction of A.S.I. No side-effects				
Excellent reduction of A.S.I. No side-effects				
Excellent reduction of A.S.I. Slight dryness of mouth				

A.S.I. = Acid Secretion Index

bathes the ulcer site, aggravating the inflammatory reaction and undoing the beneficial effects of the daytime therapy. Control of the nocturnal secretion, in a way that would not interfere with the patient's sleep and rest, would therefore be of value in obtaining more rapid and complete cure in cases of peptic ulcer.

Many anticholinergic drugs have been made available to reduce hyperacidity and hypermotility. Our studies indicate that a long-acting dosage form of hexocyclium methylsulfate will, in many cases, successfully limit the volume and acidity of nocturnal secretion in patients with and without duodenal ulcer. The results support those previously reported by Kasich and Fein[2] who demonstrated the ability of 50 mg., 75 mg., and 100 mg. of long-acting hexocyclium to maintain a relatively high gastric pH when administered at 12-hour intervals.

The medication employed for this study was hexocyclium methylsulfate long-release** (75 mg.), a special dosage form incorporating conventional hexocyclium throughout a porous plastic matrix, which is physiologically inert. Drug release is independent of pH, motility and enzyme activity, but requires only the presence of gastrointestinal fluid. These fluids are drawn into the many minute passages of the matrix so that the drug is gradually dissolved out as the Gradumet passes through the gastrointestinal tract. Thus, uniform drug activity is extended for 8 to 12 hours.

In vitro the pattern of drug release from the 50 mg. size of long-acting hexocyclium has been determined by Campbell and Theivagt[3] employing an official method with "Simulated Gastric and Intestinal Fluids"[4] with agitation. These studies demonstrated that the medication is released at the rate of 46 per cent during the first hour, another 36 per cent during the second through fourth hours, and 14 per cent during the fifth through eighth hours. The results are comparable in water at 37° C with agitation, and water at 20° with and without agitation. Drug release from the 75 mg. size follows a similar pattern, with the drug released at a rate which promotes a uniform antisecretory action.

In vivo, Kasich and Fein[2] found that gastric pH was consistently elevated, generally to values above 3.0, by 50 mg., 75 mg., or 100 mg. of the long-acting hexocyclium. Also, their clinical results in patients with duodenal ulcer and in patients with irritable colons complement the experimental results. The only side-effect noted was a mild dryness of the mouth necessitating reduced dosages in 2 of 57 patients receiving 75 mg. twice daily.

Method and Material

At one hospital (B.E.H.) 10 patients with active duodenal ulcers were selected for study. Patients with proven gastric ulcer were rejected because they frequently have low levels of free HCl and it may be difficult to rule out gastric

**Tral Gradumet® (hexocyclium methylsulfate, long-release dosage form), supplied by Abbott Laboratories, N. Chicago, Ill.

carcinoma. Although patients with active bleeding were rejected, the majority of cases did show occult blood in the stools. Nine cases were studied immediately after admission to the hospital. Only in one case was a significant number of days of conservative therapy administered. All patients who had been previously treated surgically were rejected because of the possibility of appreciable duodenal reflux. Each patient served as his own control. Supper was served at 4:30 p.m. On the evening of admission a Levin tube was introduced into the stomach at 8 p.m. The gastric contents were aspirated and discarded. The tube was then connected to a continuous suction apparatus. Five c.c. of aspirate was drawn into separate tubes at 12 midnight, 4:00 a.m., and 8:00 a.m. The total quantity aspirated from 8:00 p.m. to 8:00 a.m. was measured. The fractional and total aspirates were examined for free hydrochloric acid and total acidity, which are recorded in clinical units per 100 c.c. Gastric acidity was determined by titration with N/10 sodium hydroxide. Töpfer's reagent was employed to indicate the end-point for free hydrochloric acid and phenolphthalein for total

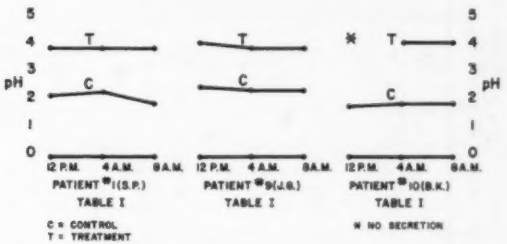

Fig. 2—Relative pH values during control and treatment periods. (Treatment with long-release hexocyclium, 75 mg.)

acidity. The Beckman glass electrode was employed for measuring pH. On the evening following the control analysis the Levin tube was introduced at 8:00 p.m. and the stomach was emptied. The patient was then given 75 mg. of hexocyclium methylsulfate long-release. Fractional and total aspirates were similarly obtained and examined as during the control period. To check for undesirable side-effects of the drug, the patients were asked whether they had excessive dryness of the mouth, visual disturbances, urinary difficulties or palpitations.

At another hospital (P.H.) 10 patients on the gastroenterologic service were selected at random. On the control night they were intubated at 8:00 p.m. No suction was applied, the gastric contents being permitted to drain by gravity into a bottle on the floor beside the bed. The stomach was not emptied. Separate specimens of 5 c.c. were collected at 8:00 p.m., 12 midnight, 4:00 a.m., and 8:00 a.m. The total quantity was measured. All specimens were examined for free hydrochloric acid and total acidity. On the test night the medication was given at 6:00 p.m. The Levin tube was introduced at 8:00 p.m. and the procedure repeated as on the control night.

TABLE II

COLLECTION BY GRAVITY

(ALL VALUES EXPRESSED IN CLINICAL UNITS PER 100 ML.)

				Control			75 mg. hexocyclium long-release			Difference			
Patient	Sex	Age	Time	Vol.	Free HCl.	Total acidity	Vol.	Free HCl.	Total acidity	Vol.	Free HCl.	Total acidity	Comments
T.H. (Gastritis) #9473	M	26	8:00 p.m.		60	127		40	100		−20	−27	Good reduction of A.S.I. No side-effects
			12:00 p.m.		2	49		0	35		−2	−14	
			4:00 a.m.		0	7		0	14		0	+7	
			8:00 a.m.		0	14		0	4		0	−10	
			Total sample	190 ml.	10	90	105 ml.	5	60	−95 ml.	−5	−30	
					A.S.I. = 19			A.S.I. = 5			A.S.I. = −74%		
E.P. (Hiatus hernia)	F	65	8:00 p.m.		48	120		60	85		+12	−35	Poor reduction of A.S.I. No side-effects
			12:00 p.m.		11	49		0	20		−11	−29	
			4:00 a.m.		20	73		5	26		−15	−47	
			8:00 a.m.		30	49		20	36		−10	−13	
			Total sample	205 ml.	21	59	180 ml.	20	70	−25 ml.	−1	+11	
					A.S.I. = 43			A.S.I. = 36			A.S.I. = −16%		
J.O'C. (Duodenal ulcer)	M	66	8:00 p.m.		20	110		6	38		−14	−72	Excellent reduction of A.S.I. Dryness of mouth
			12:00 p.m.		30	140		0	2		−30	−138	
			4:00 a.m.		42	54		0	6		−42	−48	
			8:00 a.m.		40	45		0	4		−40	−41	
			Total sample	150 ml.	18	41	50 ml.	2	20	−100 ml.	−16	−21	
					A.S.I. = 27			A.S.I. = 1			A.S.I. = −96%		
F.B. (Duodenitis) #381	M	25	8:00 p.m.		0	25		0	45		0	+20	Excellent reduction of A.S.I. No side-effects
			12:00 p.m.		14	48		0	30		−14	−18	
			4:00 a.m.		0	14		0	60		0	+46	
			8:00 a.m.		0	15		0	42		0	+27	
			Total sample	180 ml.	3	31	82 ml.	0	35	−98 ml.	−3	+4	
					A.S.I. = 5.6			A.S.I. = 0			A.S.I. = −100%		
W.C. (Duodenal	M	68	8:00 p.m.		0	15		0	16		0	+1	Excellent reduction of
			12:00 p.m.		60	105		45	87		−15	−18	

			Total sample	180 ml.	3	31	82 ml.	0	35	−98 ml.	−3	+4	
					A.S.I. = 5.6			A.S.I. = 0			A.S.I. = −100%		
W.C. (Duodenal ulcer) #5046	M	68	8:00 p.m.		0	15		0	16		0	+1	Excellent reduction of A.S.I. No side-effects
			12:00 p.m.		60	105		45	87		−15	−18	
			4:00 a.m.		30	45		3	5		−27	−40	
			8:00 a.m.		32	46		0	10		−32	−36	
			Total sample	250 ml.	36	55	100 ml.	12	24	−150 ml.	−24	−31	
					A.S.I. = 90			A.S.I. = 12			A.S.I. = −87%		
J.H. (Diverticulosis of colon)	M	65	8:00 p.m.		0	84		33	81		+33	−3	Poor reduction of A.S.I. No side-effects
			12:00 p.m.		36	110		50	110		+14	0	
			4:00 a.m.		0	82		36	80		+36	−2	
			8:00 a.m.		35	52		0	30		−35	−22	
			Total sample	180 ml.	33	93	175 ml.	40	90	−5 ml.	+7	−3	
					A.S.I. = 59			A.S.I. = 70			A.S.I. = +19%		
A.V. (Antral gastritis) #10181	F	65	8:00 p.m.		4	34		0	34		−4	0	Excellent reduction of A.S.I. Slight dry tongue
			12:00 p.m.		20	10		0	18		−20	+8	
			4:00 a.m.		0	10		0	11		0	+1	
			8:00 a.m.		0	15		0	19		0	+4	
			Total sample	115 ml.	10	35	75 ml.	0	21	−40 ml.	−10	−14	
					A.S.I. = 11.5			A.S.I. = 0			A.S.I. = −100%		
J.K. (Functional gastrointestinal disorder) #10220	F	65	8:00 p.m.		29	50		30	60		+1	+10	Excellent reduction of A.S.I. No side-effects
			12:00 p.m.		22	32		0	10		−22	−22	
			4:00 a.m.		0	8		0	8		0	0	
			8:00 a.m.		0	13		20	40		+20	+27	
			Total sample	205 ml.	25	38	110 ml.	10	30	−95 ml.	−15	−8	
					A.S.I. = 51			A.S.I. = 11			A.S.I. = −79%		
H.S. *(Hyperemesis gravidarum)* #11311	F	38	8:00 p.m.		8	69		0	4		−8	−65	Excellent reduction of A.S.I. No side-effects
			12:00 p.m.		8	90		0	17		−8	−73	
			4:00 a.m.		0	13		0	33		0	+20	
			8:00 a.m.		0	7		0	23		0	+16	
			Total sample	195 ml.	6	54	85 ml.	0	18	−110 ml.	−6	−36	
					A.S.I. = 12			A.S.I. = 0			A.S.I. = −100%		
E.W. (Gastroenteritis) #11577	F	32	8:00 p.m.		4	11		15	28		+11	+17	Excellent reduction of A.S.I. No side-effects
			12:00 p.m.		5	20		6	10		+1	−10	
			4:00 a.m.		20	38		5	18		−15	−20	
			8:00 a.m.		28	38		3	10		−25	−28	
			Total sample	220 ml.	15	25	100 ml.	5	10	−120 ml.	−10	−15	
					A.S.I. = 33			A.S.I. = 5			A.S.I. = −85%		

A.S.I. = Acid Secretion Index

Results

In order to obtain a numerical equivalent by which to estimate the effectiveness of a drug in depressing the volume and acidity of gastric secretion, we have calculated a figure which we call the acid-secretion index (A.S.I.). It is the product of volume of gastric juice secreted (in hundreds of cubic centimeters) multiplied by the clinical units of free hydrochloric acid per hundred cubic centimeters of gastric juice. A reduction of this product by 75 per cent or more is considered an "excellent" effect of the drug. A reduction of 50 to 74 per cent is considered "good". Any reduction less than 50 per cent is considered "poor".

The data for each series of 10 patients are presented separately in Tables I and II.

The data in Table I are also presented by bar graphs (Fig. 1). In this way average values for free hydrochloric acid and total acidity on the control night are compared with those from the test night for fractional and total aspirates. Average total volumes secreted on both nights are compared in a like manner.

To illustrate the change of pH values which can be achieved, control and test values for three patients are presented in Figure 2.

Comment

Of the patients studied by continuous aspiration and reported in Table I, and Figures 1 and 2, free hydrochloric acid, total acidity, and total volume were diminished throughout the 12-hour treatment period, while gastric pH was increased. The reduction of the acid-secretion index was judged excellent in 7, good in 2, and poor in 1. Suppression of secretion was generally uniform throughout the night, thus indicating a uniform therapeutic action.

The quantity of nocturnal secretion is greater among the patients tested in Table I than in Table II. All had duodenal ulcers where such secretion is known to be appreciably greater. Also, continuous gastric suction permitted complete recovery of the gastric secretion. It is possible too that constant suction may itself stimulate excess secretion, a factor which we are studying at the present time. Nevertheless, in 5 of the 10 patients there was no measurable secretion during one or other of the 4-hour intervals of the 12-hour testing period. This absence of activity occurred during the first 4 hours in 2 patients, during the middle 4 hours in 1 patient, and during the final 2 hours in 2 patients, showing that the antisecretory effect of hexocyclium and the continuous release of drug activity are maintained throughout the night. At no time was there an absence of gastric activity during the control period of any patient studied by continuous aspiration.

Gastric pH was raised (toward neutrality) by long-acting hexocyclium in all but 1 case, the increase being at least 1.0 unit in 5 cases. The change achieved in 3 cases is illustrated in Figure 2.

Of the patients studied by the gravity method and reported in Table II, the reduction of the acid-secretion index was judged excellent in 7, good in 1, and poor in 2. Both cases of proven duodenal ulcer in this group showed an excellent response. By the gravity method of collection there is an appreciable loss of fluid into the small intestine, thus accounting in part for the generally lower volumes of gastric juice noted among the patients in this group.

Among the 20 patients studied in both groups, those with and without peptic ulcer, the response as judged by the reduction of the acid-secretion index was excellent in 14, good in 3, and poor in 3. An excellent response was obtained in all 12 cases of proven duodenal ulcer.

Only 4 patients stated that they had slight dryness of the mouth. This was in no way disturbing and subsided in all instances within 4 hours after the completion of the study. No patients complained of visual disturbance, urinary difficulty or palpitation.

Summary and Conclusions

1. The effect of 75 mg. of long-acting hexocyclium on nocturnal secretion was determined in 20 patients. Ten patients were studied by continuous aspiration of gastric contents during a 12-hour control period on one night and a 12-hour treatment period on the next night. Ten others with various gastrointestinal syndromes, including 2 with duodenal ulcers, were studied by gravity collection of gastric secretion during similar control and treatment periods.

2. Volume of total content collected was recorded. Free hydrochloric acid and total acidity were determined for fractional samples at 4-hour intervals and for the total samples. The pH was also determined in the group of cases studied by continuous aspiration.

3. Data for each group of 10 patients are presented in 2 tables. Data for the 10 patients studied by continuous aspiration are further elaborated by means of bar graphs showing average values for fractional and total aspirates. Comparative pH values during the control and treatment period are presented for several of these patients.

4. The data show a pattern of drug release which appreciably suppresses the volume and acidity of the gastric secretions, as measured by the acid-secretion index, in 17 of the 20 cases. The response was excellent in all 12 cases of duodenal ulcer.

5. Side-effects were limited to slight dryness of the mouth in 4 of the 20 patients. Visual disturbance, urinary difficulty and palpitation were not encountered.

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HIATUS HERNIA AND PEPTIC ESOPHAGITIS FOLLOWING TRAUMA*

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Hackensack, N. J.

The clinical entity of esophageal hiatus hernia, sliding, and peptic esophagitis, its sequel, is well defined in medical literature[1]. Surgical procedures have been developed to reduce these hernias and prevent the disturbing reflux of gastric contents from provoking inflammatory disease of the esophagus[2]. The etiology of hiatus hernia, however, has had little attention paid to it. One reason is that for years the condition was thought to be restricted to women; pregnancy has been implicated by many authors. Undoubtedly, pregnancy and the voluntary efforts during labor are responsible for many instances of esophageal hiatus hernia (a study of the incidence in parous and nuliparous women would be interesting) but there are other causes than pregnancy. Although a congenital short esophagus is mentioned frequently in surgical literature as a cause of hiatus hernia, in practice this is a very rare finding. The short esophagus usually is more apparent than real, easily reducible and is on the contrary *a posteriori* of hiatus hernia rather than its cause. The diagnosis of short esophagus is usually made following x-ray examination. The cardioesophageal junction presents above the diaphragm and in association with a hiatus hernia of the sliding variety. This apparent short esophagus is probably due to the contraction of the longitudinal muscle fibers of the esophagus with a "give" from the mobilized proximal end of the stomach. Although the radiologic diagnosis is a short esophagus, the surgeon has no difficulty in reducing the hernia and restoring the cardia below the hiatus unless esophageal stenosis and stricture resulting from peptic esophagitis is very far advanced.

That the initial factors may be rather a weakness in the diaphragmatic crus, in the phrenoesophageal ligaments, in the so-called "intrinsic esophageal sphincters", in the angulation of the esophagus into the cardia or in other structures whose integrity maintain the competence of the hiatus, or a combination of these factors, can only be postulated at the present time.

External trauma as a cause has rarely been mentioned in discussing the etiology of this condition[3]. In the two cases presented here external trauma appeared to precipitate the characteristic symptom complex of esophagitis in association with hiatus hernia.

Although a potential muscle weakness or defect or ligamentous insufficiency may have pre-existed or the hernia itself may have been present prior to the injury (no previous gastrointestinal roentgen studies were available), symptoms were absent until the trauma occurred. If the hiatus hernia was present previous-

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ly it did not interfere with the competence of the cardioesophageal junction and this is the important fact in the production of symptoms and peptic esophagitis[4]. And although the concept that esophageal hiatus hernia may exist without reflux is inherent in some of the confusion that still surrounds the knowledge of the specific physiologic and morphologic factors that contribute to its development, this is not necessarily true. The peculiar intermittency of reflux and the evanescent quality of its symptom-complex in some patients are characteristics that require more intensive study.

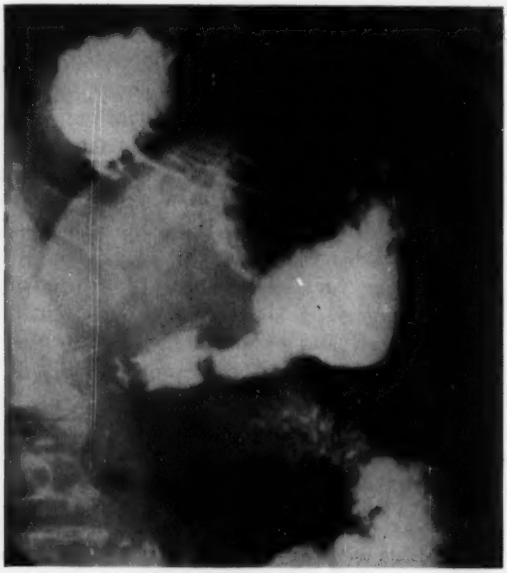

Fig. 1—Preoperative. A large gastric pouch presenting a sliding hiatus hernia is visualized. The contours of the pouch are well delineated and appear normal.

The susceptibility of a specific esophageal mucous membrane to gastric contents, the presence of heterotopic gastric mucosa in the lower esophageal segment, and the character of the acid pepsin secretion, undoubtedly are all factors that determine the gradations of the particular response, i.e., varying from symptoms without much tissue reaction to severe esophagitis with stenosis. In one patient the symptoms were marked but no radiologic evidence of inflammation was visualized. It is well known, however, that an esophagoscopic examination has often revealed moderately severe inflammatory disease without any positive roentgen findings.

Case 1:—A 51-year old white male, telephone installer, was seen for postoperative evaluation. Eight months previously he had been struck by an automo-

bile and thrown 20 ft. He was admitted to a local hospital with a fractured clavicle and bruises and contusions of the abdomen and the extremities. Twenty-four hours later, still hospitalized, he complained of heartburn while lying in bed, with occasional radiation of pain into the anterior neck. Following discharge the heartburn persisted and was associated with substernal distress and the occasional radiation of sharp pain from the epigastrium into the submandibular and glottic areas. The distress and heartburn were more frequent at night but relieved after walking about or sitting in the erect position. He repeatedly complained of symptoms to his physician and orthopedist. (There was no past history of any previous gastrointestinal distress.) After three months of

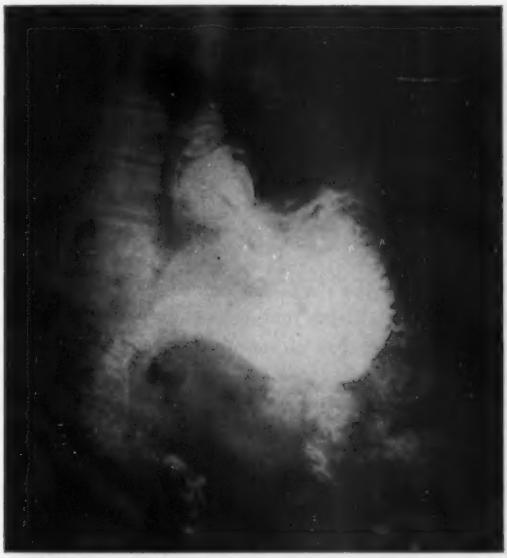

Fig. 2—Postoperative. The esophagus is adequately distensible and shows no evidence of inflammation. The gastric pouch is smaller but the hiatus hernia is well visualized. Reflux could not be provoked.

acute discomfort a barium meal examination was performed and a large sliding hiatus hernia 7 x 6 cm. was visualized (Fig. 1). The hernia was incompletely reduced in the erect position. No esophageal inflammation was noted. Medical therapy did not relieve the symptoms and he was operated on several months later for the repair of an esophageal hiatus hernia. At laparotomy there was slight induration of the tissues around the distal third of the esophagus. Following surgery, the heartburn and substernal pain rapidly disappeared although the postoperative films revealed incomplete reduction of the gastric pouch (Fig. 2). No further therapy was recommended.

Case 2:—A 63-year old Sacristan was referred with a history of heartburn and sour regurgitation of four months' duration. At the onset of his present illness he had fallen from a ladder, landed prone fracturing his left arm and injuring his abdomen and back. He was hospitalized and an open reduction of the arm was necessary to repair the injury. Two days following the surgical procedure (without gastric intubation) he began to complain of sour regurgitation and heartburn. This occurred usually 30 minutes to 2 hours after meals and was accompanied by upper abdominal distress and pressure in the substernal area. Sour regurgitation of water brash usually followed large meals. Heartburn and regurgitation were the invariable accompaniments of stooping or bending forward after a meal. Physical examination was essentially negative except for a scar on the left arm and bilateral, indirect inguinal hernias. A gastric analysis revealed no free hydrochloric acid in a fasting specimen but 36 clinical units following a basal (.5 mg.) dose of histamine. A barium meal examination was performed. The esophagus was shortened and the contours of the lumen of the distal third were fuzzy. A hiatus hernia of the sliding variety measuring 4.5 x 6 cm. was visualized, completely reducible in the erect position. Reflux of gastric contents was prompt and could be initiated by abdominal compression in the supine position or provoked by the Johnstone maneuver. Symptoms were readily reproducible by these maneuvers; reflux of gastric contents provoked heartburn and sour regurgitation. Esophagoscopic examination revealed a moderately severe inflammation of the distal 4-5 cm. of esophageal mucosa particularly on the left lateral wall. A whitish mucoid exudate was observed but bleeding could not be easily provoked. No ulceration was visualized. The diagnosis was sliding esophageal hiatus hernia with moderately severe esophagitis, posttraumatic. The patient improved on an antacid regimen and the usual instructions for the treatment of hiatus hernia. He declined surgery.

Conclusion

External abdominal trauma is presented as the cause of hiatus hernia and peptic esophagitis or of peptic esophagitis following a pre-existing hiatus hernia. Two patients who devloped symptoms of peptic (reflux) esophagitis within 48 hours of trauma are reported.

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FULMINANT GASTROENTERITIS

Case Report

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A grave clinical syndrome characterized by sudden onset of nausea, vomiting, diarrhea and rapidly developing prostration is being recognized with increasing frequency. A high mortality incidence is associated. Occasionally this syndrome has been noted postoperatively. Most cases reveal pseudomembrane present in the fecal material with numerous staphylococci on direct smear and coagulase-positive staphylococcus isolated on culture. In occasional cases pseudomembrane is not found and the diagnosis is left in more doubt. The following case report illustrates the dramatic rapidity of the cholera-like clinical picture, and is unusual with the remarkably diffuse necrotizing mucosal lesion of the gastrointestinal tract without acute inflammatory exudate in the remaining layers of the intestinal wall occurring before antibiotic administration.

A 52-year old white, male, printer was hospitalized on 20 April 1956 for nausea, vomiting and diarrhea that began suddenly on the day previous to admission while on his way to work. He denied having eaten anything unusual and there was no similar illness in the family or among his co-workers. The patient had two teeth extracted by his dentist four days prior to the onset of the present illness without complication and not requiring the use of antibiotics. When the diarrhea persisted, the patient, at the suggestion of his dentist, was given 200,000 units of oral penicillin 12 hours after the onset, and a local physician administered combiotic and antispasmodics. The patient became so markedly prostrate with intractable, painless diarrhea, consisting of copious, brown, thin, watery fecal material that hospitalization was necessary. The past history revealed only an unverified diagnosis of polycythemia made 20 years previously and not requiring therapy or follow-up. There was a mild, transient, uneventful attack of diarrhea six months before admission, subsiding spontaneously. The family history and review of systems were essentially unrevealing.

On admission, the patient showed marked dehydration and ashen cyanosis. He was mentally and physically sluggish but cooperative and oriented. The pulse rate was regular at 100 per minute, the temperature rectally 100.6 degrees F,

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the blood pressure was 90/70. The eyeballs were soft to palpation. The pharynx was hyperemic. The chest, lungs and heart were within normal limits on examination. The abdomen was soft and showed no rebound-tenderness or palpable masses. The remainder of the physical examination was within normal limits.

The urine revealed a specific gravity of 1.021; acid reaction, 1 plus; albumin, trace of sugar; leucocytes and many hyaline casts. The red blood count revealed 5.9 million red cells; 17.5 gm. hemoglobin; 5,000 white cells with 72 segmented; 2 stab forms; 21 lymphocytes and 5 monocytes. Biochemical blood findings showed 118 mEq. chlorides; 133 mEq. sodium; 5.2 mEq. potassium.

Fig. 1—Small intestine with necrosis and inflammatory infiltrate limited to mucosa; marked vasodilatation of submucosa; muscular coats normal (x64).

The treatment initially consisted of a regimen of fluid-electrolyte replacement, nothing by mouth, and 2 c.c. of combiotic given to supplement that of his local physician. About 16 hours after admission, the patient felt slightly better. The blood pressure was 110/70, the temperature 105.6° F; the vomiting subsided but the diarrhea persisted. Paregoric was given orally as well as small doses of morphine to control the diarrhea and aspirin and alcohol sponges to control the pyrexia. Rectal examination at this time revealed mucosal edema and the presence of blood. About 22 hours after admission vomiting recurred.

The patient complained of sore throat; oral medications and fluid were discontinued and intravenous fluids resumed. He became lethargic and the temperature varied between 102 and 105°. Chloromycetin was given pending the bacteriological stool study. At that time the hematocrit was 59 volumes per cent; red count, 6.2 million; hemoglobin, 17.8 gm.; white count, 12,000 with 68 segmented forms; 16 stab forms; 12 lymphocytes and 4 monocytes. The other findings included chlorides of 124 mEq.; sodium, 145 mEq.; potassium, 4 mEq.; urea nitrogen, 2.19 mg. per cent. Stool culture showed no enteric gram-negative pathogens, direct smear of stool showed gram-positive cocci in predominance. The blood culture was sterile after 48 hours. Serological studies were negative for typhoid O and H, paratyphoid A and B, brucella and proteus OX 19.

About 30 hours after admission the patient went into shock. There was little or no response to parenteral digitalis, intramuscular neosynephrine, corti-

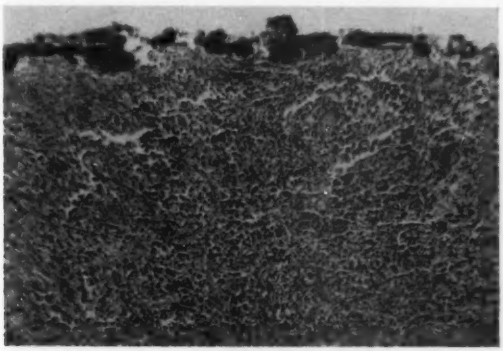

Fig. 2—Bacterial colonies on surface of necrotizing mucosa with mononuclear inflammatory cells (x350).

sones, ACTH and intravenous levophed. A total of 11 liters of intravenous fluid had been given. Membranous particles were noted in the fluid stools. The patient expired 37 hours after admission, or approximately 61 hours after the onset of his illness.

Synopsis of significant autopsy observations (3 hours after death):—The gingiva of the right and left maxilla showed small healing postextraction wounds, not cultured. A persistent, prominent thymus was present. The peritoneal cavity contained 400 c.c. of clear, pale, amber fluid. Both lungs were atelectatic. The heart weighed 300 gm. and the myocardium was flabby. The esophageal mucosa was congested. The stomach was slightly dilated, the wall thinned, the mucosa congested and 250 c.c. of thin, sanguineous fluid was present in the lumen. The small intestine was reduced in calibre, that of the terminal ileum measuring 1 cm.; the wall throughout felt edematous. The serosa was smooth and glistening. From the duodenum to the ileocolic valve the intestinal mucosa showed diffuse

areas of shallow ulceration with sharp borders and smooth pallid base. Variable sized, coiled fragments of necrotic, yellow-green membranous structure were found throughout the lumen of the small intestine. The long diameter of the ulcerations was generally parallel to the longitudinal axis of the bowel.

The intervening intact mucosa was congested. The mucosa of the appendix was swollen and bosselated in appearance. The large bowel showed congestion and swelling of the mucosa. No enlarged nodes were found in the mesentery.

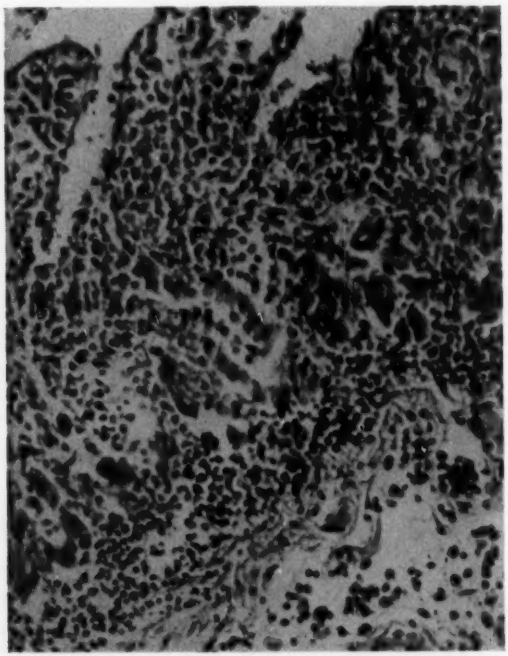

Fig. 3—Intense mononuclear inflammatory infiltrate of mucosa of small intestine with beginning disintegration of glandular units, and dilated vessels with many mononuclear cells in the submucosa (x500).

The liver weighed 1,525 gm. and was soft in consistency. The spleen weighed 140 gm., was soft and dark-red. The kidneys weighed 135 and 140 gm., were swollen and pallid on section. The prostate was moderately enlarged. The adrenals were soft in consistency.

Microscopy of gastrointestinal tract:—Vasodilatation in the submucosa is marked in all segments of the digestive tract (Fig. 1). A minimal leiomyoma is found in the submucosa of the gastric cardia. The stomach shows areas of superficial mucosal necrosis with plasma cell infiltration and bacterial clumps.

Sections of pylorus, duodenum, jejunum and ileum show striking changes in the mucosa and submucosa (Figs. 1, 2 and 3). The tips of villi and summits of mucosal folds show necrosis which extends down into the mucosal crypts. The areas which are denuded of mucosa show an intense leucocytic infiltrate of mononuclear cells and only a rare polymorphonuclear leucocyte. The inflammatory process is consistently limited to the mucosa and often to the upper two-thirds or less (Fig. 1). Large masses of gram-positive bacteria are present on the surface of the lesions (Fig. 2). Bacteriology of a jejunal ulcer reveals on direct smear, excessive gram-positive cocci, and on culture, hemolytic staphylococcus aureus, coagulase positive; sub-typing was unavailable.

The large intestine shows superficial mucosal desquamation and increased plasma cells in the mucosa. The liver and kidney show marked toxic swelling of parenchymal cells.

The chief anatomic diagnoses are: Necrotizing gastroenteritis and healing gingival extraction wounds.

Comment

The literature is replete with case reports exhibiting this violent pattern of cholera-like diarrhea which rapidly becomes fatal. The complex terminology indicates the uncertainty of etiology. Pseudomembranous, diphtheritic and membranous enteritis, enteritis necroticans and staphylococcal enteritis are some of the commonly encountered terms. The names are, for the most part descriptive and do not refer to cause.

The fact that Finney[1] in 1893 noted a similar case in a postoperative gastrectomy patient indicates that antibiotics are not an essential causative factor in all cases. The occurrence of such cases in association with use of antibiotics in recent years may be coincidence rather than cause. The widespread use of antibiotics and the relatively low incidence of this syndrome gives support to this view. In the present case diarrhea began before the administration of antibiotics and the amount he received was not large prior to the development of severe symptoms and evidence of shock.

In the usual case with obvious pseudomembrane, there is pronounced polymorphonuclear leucocyte reaction in the intestinal wall. The remaining areas of mucosa reveal polymorphonuclear infiltration of marked degree. This case has a striking lack of polymorphonuclear infiltration. The organisms were in abundance within the lumen. This type of case is not uncommonly encountered in the literature, particularly from Great Britain. The response may be a local response to staphylococcal toxin. The ultimate acceptance of this organism group as causative agents will depend upon the demonstration of the conventional postulates.

Zeissler and Rassfeld[2] isolated type F *Cl. welchii* in special studies on material from cases observed in an epidemic in Germany. In view of the great

variations in intestinal flora, further studies of the role of this organism would be required prior to its acceptance as a possible incitant. Fick and Wolkin[3] also noted associated aerobic organisms.

Williams and Pullan[4] reported ten similar cases including five fatalities with sloughing of the mucosa in every case examined at autopsy. Histologically, the lesions were limited to the mucosa with relatively normal submucosa. Cellular infiltrates consisted of histocytes and lymphocytes; polymorphonuclear leucocytes were scarce. Shock was the most constant clinical feature especially in fatal cases. In this series, stool cultures of 5 fatal and 2 nonfatal cases revealed staphylococcus aureus in four cases, two of whom survived. In the remaining three, all fatal, hemolytic streptococcus was isolated in one, *Bacterium mucosum capsulatum* in the second, and one *B. proteus* in the third.

Because of the extensive picture of necrosis frequently noted following abdominal surgery, Penner and Bernheim[5] suggest a major role for shock with resultant local vascular spasm and ischemia. They hypothesize that these in turn produce the massive tissue necrosis. This mechanism is seen also in the pituitary gland and renal cortices. It is questionable whether shock, *per se*, could produce such necrosis, without additional local factors. In the case reported herein, as in many others, there was no element of pre-existing shock.

It appears that no one factor adequately explains all of the cases of necrotizing enteritis. It may well be a type of host response to a local and/or systemic overwhelming stress.

Results of therapy reported by Williams and Pullan[4] are widely accepted. Massive fluid therapy is a "must". One case recovered after requiring 10 liters of intravenous fluid within three hours. Shock should be vigorously treated with fluids, plasma expanders and vasoconstricting agents. Early use of steroids might well be of benefit in the presence of shock.

Summary

A fatal case of fulminating cholera-like diarrhea is presented with necropsy findings which reveal a nonpyogenic tissue reaction despite recovery of coagulase positive staphylococcus aureus. A brief discussion of the surveyed literature is presented.

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THE CLINICAL EVALUATION OF A NEW LONG-ACTING ANTICHOLINERGIC DRUG

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Introduction

New pharmaceutical products for the treatment of gastrointestinal hyperactivity appear at frequent intervals. This vigorous search for and production of new parasympatholytic drugs is, in a great part, due to the fact that no perfect or fully adequate drug is as yet available. An anticholinergic drug with proven prolonged activity is still missing from the physician's armamentarium. While during his waking hours, the frequent intake of food and antacid can neutralize the patient's gastric acidity, nocturnal hypersecretions can be controlled without awakening the patient only by an effective long-acting antisecretory drug taken before bedtime. Therefore, such a drug is very desirable.

Laboratory reports[1,2] indicated that the use of drug ion exchange resin complexes might produce a long-acting drug having a low order of toxicity. It seemed worthwhile to apply this principle to antisecretory drugs and to evaluate their clinical efficacy in the prolonged suppression of gastric secretion in man. Methylscopolamine as an ion exchange resin complex is this type of medication to be evaluated in this report. It was employed with and without the addition of a new sedative 2-methyl-3-orthotolyl-quinazolone as an ion exchange resin complex.

Materials

Capsules of identical appearance were used. They were known as SG1 and SG2 and contained the following:

SG-1 10 mg. methylscopolamine as an ion exchange resin complex.

SG-2* 10 mg. methylscopolamine and 40 mg. of 2-methyl-3-orthotolyl-quinazolone as ion exchange resin complexes.

Method

The effect of the above drugs on the acidity of the gastric juice was evaluated in 54 hospitalized patients ranging in age from 26 years to 78 years, with a median age of 64. They had a variety of diseases including diabetes, hypertension, rheumatoid arthritis, multiple sclerosis, paraplegias, cerebral vascular

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*This mixture is available as Akalon-T from the R. J. Strasenburgh Co.

accidents, carcinomatosis, acromegaly, dermatoses and emphysema, but excluding known gastrointestinal disease.

The degree of gastric acidity in these patients was estimated by the Azure A Carbacrylic Resin Diagnostic Test (Diagnex Blue Test)[3,4]. An initial urine was discarded at 6 A.M., at which time two caffeine tablets were taken. At 7 A.M., the control urine was collected and the carbacrylic resin was taken by the patient with one-half glass of water. At 9 A.M., the final urine specimen was collected. It was immediately tested according to the procedures outlined by Segal, Miller and Plumb[3]. The final colorimetric comparison was done after

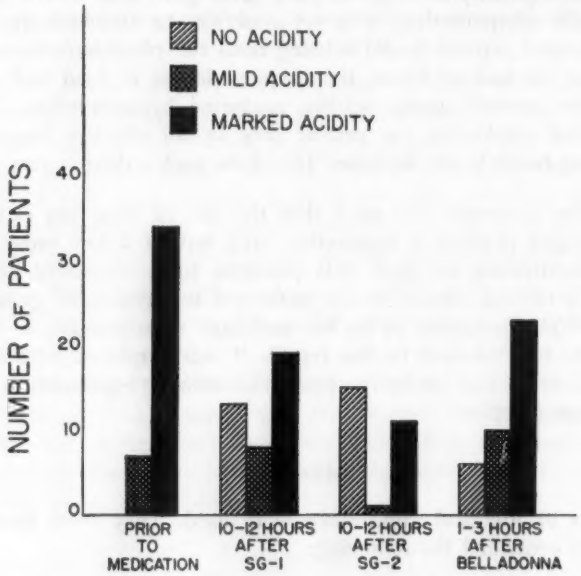

Fig. 1—Showing the responses of patients to the medications as measured by Azure A Carbacrylic Resin Diagnostic Test.

acidification, boiling and cooling of the urine. The results were recorded in terms of anacidity or free acidity.

All 54 patients were tested before the drug trials by this method for free acidity; those who showed no acidity were retested without further medication. Those patients who had free acidity, were retested at weekly intervals with coded preparations SG1, SG2 or tincture of belladonna in random order. The SG1 or SG2 was administered at 9 A.M. and 9 P.M. on the day prior to the test. The belladonna (ten drops with one glass of water) was given at 6 A.M. on the morning of the Diagnex Blue Test. All patients were checked for subjective symptoms.

Results

Thirteen of the original 54 patients proved to have initial achlorhydria and remained anacid on repeated testing with Diagnex Blue and were not further tested. The remaining 41 patients who had varying degrees of free gastric acidity were retested after medication with the test drugs. Ten to 12 hours after SG1 medication, 13 out of 41 patients (32 per cent) showed anacidity; ten to 12 hours after SG2 ingestion, 15 out of 27 subjects (56 per cent) had gastric achlorhydria; 1 to 3 hours after belladonna only 6 out of 40 patients (15 per cent) demonstrated anacidity (see Table I).

Thus SG2, the resin complex containing both the anticholinergic and sedative medications had the most marked acid-suppressing effect, demonstrable even 10 to 12 hours after medication. Belladonna, even at its assumed peak of physiological efficacy was less effective than either SG1 or SG2.

TABLE I

Responses of 41 Patients to the Medications as Measured by Azure A Carbacrylic Resin Diagnostic Test

Medication	Time ingested prior to testing	Positive for gastric acidity	No free gastric acidity	% of patients anacid
None	—	41	0	0
SG1	10-12 hours	28	13	32
SG2	10-12 hours	12	15	56
Drops ten Belladonna	1 - 3 hours	34	6	15

Side-effects

Two women in adjoining beds had flushing and erythema of the face following both SG1 and SG2 ingestion. Two elderly males developed urinary obstruction; both had benign prostatic hypertrophy and difficulty in urinating prior to this testing. No other side-effects were noted.

Comment

Our aim in this study was to evaluate SG1 and SG2 objectively as to their physiological and side-effects. A marked suppression of gastric acidity after the use of the SG2 and also SG1 as compared both to the control period and to the use of belladonna was demonstrated with the Azure A Carbacrylic Resin Diagnostic Test. In the elderly patients without gastrointestinal disease, this medication was not only somewhat more effective than the belladonna, but actually the superior effect continued for 10 to 12 hours after ingestion of the SG1 and SG2 as compared to the belladonna effect which was measured at one

to three hours after medication. A more effective therapeutic result could doubtlessly be achieved by adjustment of the dosage of the medication to the individual patient's sensitivity, need and tolerance[4]. In none of these hospitalized patients was the medication given for more than two consecutive doses, nor was the dosage individually adjusted or increased to symptoms of toxicity or to the point of salivary inhibition.

We have also treated 23 clinic patients with SG1, SG2, and placebo therapy in an attempted double-blind study. Because of the insurmountable difficulty in evaluating the effectiveness of this type of medication in such uncontrolled circumstances, no definitive effective objective conclusions could be drawn. It can be stated, however, that these 23 patients took each of the medications, one at a time, twice daily for a week without side-effects. Seven further patients who were evaluated by nocturnal gastric aspirations also tolerated the medication even in double dose without side-effects.

Thus, of all these 71 patients, side-effects were noted in only four (6 per cent). Two of these were elderly males with known benign prostatic hypertrophy who had difficulty urinating prior to this study, and following the use of the medication required catheterization. Ephemeral erythema and flushing of the face was noted in two female patients in adjoining beds. Both types of side-effects were typical of the atropine group of drugs.

Summary

A new sustained release anticholinergic drug with and without sedative in resin form was evaluated. Suppression of gastric acidity could be demonstrated 10 to 12 hours after medication in 32 per cent of patients after SG1 and in 56 per cent after SG2. Minor side-effects of the atropine type were noted in 6 per cent of patients.

Acknowledgment

The author desires to acknowledge the advice and encouragement which he received from Dr. Martin G. Goldner, Director of Medicine, Jewish Chronic Disease Hospital.

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PHLEGMONOUS GASTRITIS*

Report of an Additional Case

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Since the Middle Ages and probably earlier, physicians have recognized the entity of acute phlegmonous gastritis also described as "carbuncle" or "erysipelas" of the stomach. The condition is rare and has been a matter of academic interest, the mortality rate ranging in the neighborhood of 90 per cent. Only 335 cases had been reported in the world literature up to 1946[1]. During the past 20 years an average of one article per year, related to this subject, has appeared in the English language journals. With the advent of chemotherapeutic agents and antibiotics, the disease has become a rather rare curiosity which many surgeons and pathologists have never encountered.

The pathological process consists of an exudative fibrinopurulent inflammation of the full thickness of the gastric wall involving particularly the submucosa. The inflammation often begins at the site of a corrosive or ulcerative mucosal process and consequently may be associated with carcinoma or peptic ulcer. Many times, however, the mucosa is apparently intact and in these cases the process is sometimes associated with a distant focus of infection, particularly in the oropharyngeal region. Some cases occur as a result of a state of bacteremia[2,3] or following local surgical procedures. An association with a hypochlorhydric state as in atrophic or alcoholic gastritis has also been noted and may be attributed to the lack of the usual repressive effect on bacterial activity of the acid content of gastric juices.

Grossly, the wall of the stomach is thickened in a diffuse fashion by the inflammatory process. There is massive infiltration by neutrophils enmeshed in fibrinous material occasionally forming focal abscesses (carbuncle). Rare cases presenting a pronounced necrosis have been described sporadically and termed *necrotizing* gastritis. A recently reported case of this type followed an acute ulcerative stomatitis caused by fusospirochetal bacteria[4]. In the vast majority of cases the hemolytic streptococcus has been identified as the etiological agent. Generally, two pathological forms are recognized.

1. *Localized* showing focal involvement of the stomach wall, often with the development of perigastritis complicated by formation of a subhepatic

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abscess and usually leading to formation of adhesions. Signs of gastric obstruction may result from the compressive effect of an abscess, particularly of one located near the antrum. The perigastric abscess may heal following perforation and drainage into the gastric lumen, or the contents of the abscess cavity may be evacuated into the peritoneal cavity producing a secondary peritonitis.

2. *Diffuse* and more common form generally pursues a fulminating course with death due to generalized peritonitis. This may occur with or without, perforation and is usually associated with symptoms of septic toxemia.

The inflammatory process in many cases is sharply limited to the stomach with no alteration in adjoining esophagus and duodenum. This, however, is not constant and sometimes these structures are involved. Inflammatory changes at the ampulla of Vater may lead to obstructive jaundice. A rare case of primary

Fig. 1—Gross appearance of opened stomach and contiguous portion of esophagus and duodenum.

duodenal, or less often esophageal involvement has also been described. Cases in which there has been opportunity to do fluoroscopy studies have shown gastric atony with loss of mucosal pattern and retention. The picture may simulate a large neoplastic lesion.

Phlegmonous gastritis is somewhat more prevalent in adult males. The symptoms in the diffuse form are those of acute abdominal disease with sepsis. Severe, rather localized, continuous epigastric pain is present generally showing no tendency to radiation. The onset is usually abrupt and sometimes associated with chills and complaints of excessive thirst. Vomiting is frequent as well as elevated temperature, tachycardia and leucocytosis. Occasional cases show leukopenia indicating poor response or overwhelming of body defense mechanisms. Some patients obtain relief of the abdominal pain in a sitting up position

(Deininger's sign). Later, an exudative pleuritis, or less commonly pericarditis, has been noted. Finally, with the progression of peritonitis, the abdominal pain becomes generalized and is associated with marked tenderness, rigidity, hyperperistalsis and eventually absence of bowel sounds.

The diagnostic criteria in the diffuse form are not constant, but are rather typical. Failure to diagnose the entity is usually due to unfamiliarity with it

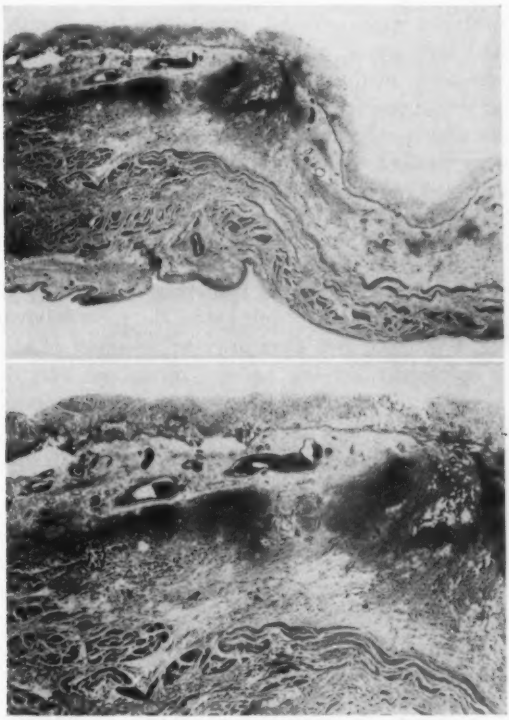

Fig. 2—*Top*, low, and *bottom*, medium power views of stomach wall showing the dense accumulations of neutrophils and thrombosed veins involving predominantly the submucosa.

on the part of the clinician. In these cases the diagnosis is usually established at postmortem or at time of exploratory laparotomy. Among the more common diseases simulating an acute phlegmonous gastritis clinically are acute pancreatitis, perforated peptic ulcer and cholecystitis.

Therapy consists of supportive measures and antibiotics. Nasogastric suction is valuable, presenting a possible form of drainage in those cases where abscess formation has occurred. In localized, subacute forms with a perigastric abscess,

healing may occur by spontaneous or surgical drainage of the abscess. Segmental resection of the stomach is usually indicated in these cases. It is doubtful whether any operative intervention is indicated in the diffuse form. An insufficient number of cases, however, has been treated by extensive resection to determine the efficacy of such treatment in the early stages of this disease.

A recent report of three localized cases of phlegmonous gastritis (one involving a gastroduodenostomy, one of the greater midcurvature and one of the "gangrenous" type) has appeared[5]. All were successfully treated with penicillin. In one case, local infiltration with penicillin was used to form an antibiotic barrier against extension of the process. In another case, the "gangrenous" portion was plicated by seromuscular inverting suture to exclude the disease from contact with the peritoneal cavity. Since antibiotic agents prevent extension of the inflammatory process across an anastomotic line and stoma, so also would they not limit localized nonoperated lesions? It is interesting to speculate, however, whether the above cases would have recovered without the associated surgical intervention.

Case report:—A 64-year old Negro man was admitted to the hospital complaining of severe epigastric pain of ten hours' duration following the ingestion of a cup of coffee. For about two days prior to the onset of acute symptoms he had noted mild epigastric distress, nausea, occasional vomiting, and general malaise. For a period of a few hours just prior to admission, he had vomited a few times and described the initial vomitus as resembling coffee grounds. The past history was entirely negative. The patient denied any alcoholic intake and stated that he had always enjoyed good health.

Physical examination showed a well developed, well nourished man in moderately acute distress from abdominal pain. Pertinent physical findings included a blood pressure of 150/90, a pulse of 84 and a temperature of 99°F. The mucous membranes of the mouth were dry and the tongue had a whitish coating. The abdomen was soft, but tender and slightly rigid in the epigastrium. The bowel sounds were normal.

The white blood count on admission was 8,200 with 85 per cent neutrophils and 15 per cent lymphocytes. Hemoglobin was 13.6 gm. with a hematocrit of 42 per cent. Urinalysis showed 3 plus sugar and a trace of albumin. Serum amylase was 102 units, glucose 407 mg. per cent. Calcium was 9.1 mg. per cent, direct van den Bergh 0.4 mg. per cent with a total of 1.2 mg. per cent. A repeat determination of glucose on the same day was 434 mg. per cent with an amylase level of 38 units.

Differential diagnosis on admission was acute localized peritonitis due to acute pancreatitis with cholecystitis and gastritis to be ruled out. The patient was given sedation and intravenous fluids and Achromycin (tetracycline hydrochloride). A Levin tube was inserted for gastric suction.

On the second hospital day the blood glucose rose to 540 mg. per cent, and urinalysis showed 4 plus glucosuria and strongly positive acetone. It was felt that the patient had acute diabetes due to an acute necrotizing pancreatitis, although there was no elevation of serum amylase to support this conviction. He was started on insulin therapy which resulted in a slight drop in his blood sugar level. The patient showed a steady rise in his temperature reaching a level of 104°F, with a pulse of 120-140/minute. In addition, although the abdomen was still soft, there was hypoperistalsis with an extension of the pain and guarding to the periumbilical region and left lower quadrant of the abdomen. A flat plate of the abdomen showed gaseous distention of two small bowel loops in the right upper quadrant ("sentinel" loops). The patient also developed a left pleuritis.

By the third day the patient was in a state of shock, administration of Levophed (levarterenal bitartrate) failing to maintain his blood pressure. At the same time he showed severe oliguria. Laboratory data at this time showed a serum amylase of 33 units, serum calcium of 9.0 mg. per cent, BUN of 36 mg. per cent; CO_2 of 23 mEq. and normal serum electrolytes, hemoglobin and hematocrit. The abdomen was now distended, tympanitic and diffusely rigid denoting progressing peritonitis. In addition, there was evidence which suggested that a right-sided pleuritic process was also present. An abdominal puncture was performed and yielded 200 ml. of cloudy, amber fluid which was negative for amylase and lipase. Smear of the peritoneal fluid showed streptococci. The organism, however, could not be cultured probably because the patient had received intravenous Achromycin (tetracycline hydrochloride).

On the fourth hospital day the patient became stuporous and expired.

Autopsy findings:—The pertinent findings at autopsy were largely limited to the abdomen. The peritoneal cavity contained about 500 ml. of a cloudy, pinkish-tan fluid with fibrin deposited on the serosal surface of the intestines, but especially the stomach. The stomach wall showed a moderate degree of diffuse thickening and was extremely soft and pliable. The mucosal rugal pattern was almost completely lost, only a few broadened rugae still being discernible. The mucosa presented a rather smooth to finely corrugated and glistening, dark red-tan to yellow-tan appearance. The mucosa at several points was interrupted by superficial, sharply outlined, ovoid ulcers 2.0 to 8.0 mm. in diameter (Fig. 1). The cut surface of the stomach wall had a moist finely spongy appearance with obscuration of the muscle coats. The esophageal wall showed similar changes, but to a lesser degree.

Microscopically, the esophagus and stomach showed throughout all layers, but most prominent in the submucosal zones, large numbers of densely packed neutrophils occasionally intermixed with granular, cellular debris enmeshed in varying amounts of fibrinous material. In a few focal areas the neutrophils were present in such heavy concentration that they completely obscured the

underlying architecture suggesting early abscess formation. Many of the submucosal veins contained recent thrombi (Fig. 2). The esophageal mucosa was interrupted by many ulcers lined on their luminal aspects by thin, pyogenic membranes. The smooth muscle bundles of the stomach and esophagus were separated one from another by the accumulations of neutrophils, and lying on the serosa of the stomach was a thin, fibrinous exudate.

The small bowel, especially the duodenum, showed a mild peritonitis and occasional scattered neutrophils throughout their walls. The mucosa was everywhere intact and the ampulla of Vater easily probed.

Additional autopsy findings of interest included a lower nephron nephrosis, microscopic foci of carcinoma of the prostate, bilateral fibrinous pleuritis, and in the upper pole of the left kidney a mild pyelonephritis. The pancreas was normal, both grossly and microscopically. There was a moderate fatty metamorphosis of the liver, which in view of the state of hyperglycemia, may have been related to increased hepatic glycogenolysis and gluconeogenesis induced by the septic toxemia.

Summary

A case of phlegmonous gastritis is presented which shows, in addition, lesser involvement of the esophagus and the small bowel. The diffuse inflammatory response noted in the involved organs was rather characteristic of a streptococcic infection which terminated with a fatal septic toxemia.

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President's Message

A Well Planned Program Is Not Enough

The convention program is ready. It is well planned and should interest the gastroenterologist, the internist, the surgeon, the radiologist, and the general practitioner.

A well planned program is a basic requirement in any type of meeting, but a vital element in its success is good attendance.

At the recent meeting of the American Medical Association, I attended the section meeting of gastroenterology and proctology and while the scientific program was excellent—the finest in many years, the attendance was pitiful. In one session, I counted thirty people in the audience. The excellent program was worthy of a full house.

Plan to attend our convention and help make it a success! Come and meet your friends, attend some social functions and at the same time you will have an opportunity to participate in fine scientific meetings and view interesting and educational scientific exhibits.

You will return to your home refreshed and stimulated, and with renewed vigor carry on your activities.

Jos. Shaiken

Fellowship Keys

Keys for *Fellows* of the American College of Gastroenterology have been authorized by the Board of Trustees. An illustration of the key is at the left.

These may be ordered from the headquarters office, 33 West 60th Street, New York 23, N. Y., at $10.00 each including federal tax and shipping charges.

The reverse side of the key will be engraved with your name and the date of your election to Fellowship. Send your order today.

In Memoriam

We record with profound sorrow the passing of Dr. Henry J. Vier, White Plains, N. Y., Associate Fellow of the American College of Gastroenterology. We extend our deepest sympathies to the bereaved family.

ABSTRACTS FOR GASTROENTEROLOGISTS

ESOPHAGUS

X-RAY DIAGNOSIS OF DISEASES OF THE ESOPHAGUS: C. Allen Good. Wisconsin M. J. 58:157 (Mar.), 1959.

The author describes in detail various methods of x-ray examination of the esophagus for adults and infants. Congenital anomalies of the esophagus are described and methods of diagnosis by x-ray are discussed.

Extrinsic masses, strictures, hiatal hernia, cardiospasm, esophageal varices and tumors malignant and benign are all carefully described.

It is good for both the internist and the surgeon to read this paper and realize the difficulties that the radiologist encounters when he has a patient with some esophageal anomaly and tries to help the referring physician confirm a diagnosis.

ABRAHAM BERNSTEIN

STOMACH

THE PATHOGENESIS OF PEPTIC ULCER: Lester R. Dragstedt. Illinois M. J. 115:68 (Feb.), 1959.

Peptic ulcer at duodenal site results from hypertonic vagus stimulation of gastric glands, rapid emptying into duodenum of excessive acid; gastric ulcer from hypotonic vagus stimulation, food stasis, prolonged antral contact or from secondary stenosis of pylorus that has all characteristics of hypotonic vagal stimulation.

J. EDWARD BROWN

SEVERE DEFICIENCY FOLLOWING SUBTOTAL GASTRECTOMY: M. Conte, J. Ristelhueber, J. Dalayeun, B. Lagente and P. Jaulin. La Semaine des Hopitaux, p. 451 (12 Feb.), 1959.

On the basis of 7 personal cases, the authors review the clinical and biological data concerning the severe deficiency syndrome in gastrectomized subjects.

The deficiency may occur after a long time (16 years in 2 of the 7 cases). Preliminary evidence is given by an extreme asthenia and a loss of body weight. Diar-

rhea precedes the edemas, but these may be absent. There are usually involvement of the exoskeleton and enlargement of the liver, occasionally some skin elements of purpura type.

Anemia is usual with diminution of the blood volume and shortening of the erythrocytes life; fall in total protides, especially in serum albumin, is constant.

In severe cases the "calorico-nitrogen" balance proves negative. The pathogenesis is explained by a diminution of the nutritive supply and absorption by the mucous membrane of the small intestine, probably related with an atrophy of the jejunal mucosa.

The treatment consists in blood transfusions and prolonged both hypercaloric and hyperprotidic diet.

MALIGNANT STOMAL OBSTRUCTION FOLLOWING SUBTOTAL GASTRIC RESECTION: Gordon F. Madding. Am. J. Surg. 97:326 (March), 1959.

This presentation is given to emphasize a method of providing decompression for the patient in whom an obstruction develops after gastric resection for malignancy.

It is recommended that double jejunostomy be performed. The proximal jejunostomy tube is inserted into the jejunum approximately 8 inches distal to the gastroenterostomy stoma. It is threaded up through the jejunum to the anastomosis and through the obstructing tumor into the gastric remnant. If necessary, the tube may also be threaded into the lower end of the esophagus, if impingement upon this has already taken place. If the obstruction involves the proximal loop of jejunum as well, the catheter is inserted through the loop of the jejunum into the stomach in the aforementioned manner. This procedure provides for decompression of both the proximal limb of the jejunum as well as the stomach and esophagus. A second jejunostomy tube of the same caliber is placed into the distal limb of the gastroenterostomy, approximately 10 inches distal to the anastomosis.

These tubes provide a simple, safe and effective method of drainage of the gastric pouch and or esophagus. It obviates the need for use of the nasogastric tube. Third, an avenue is provided so that all feedings and secretions may be removed from the obstructed gastric pouch, or proximal limb of the gastrojejunostomy as the case may be and then reintroduced into the distal jejunum. Furthermore, food, fluids and medication may be introduced into the distal jejunum obviating the necessity for parenteral therapy.

CARL J. DEPRIZIO

PERFORATED DUODENAL ULCER IN A 2,100 GRAM FEMALE INFANT, WITH SURVIVAL: John E. Lyday, Marguerite Markarian and Jonathan E. Rhoads. Am. J. Surg. 97:346 (March), 1959.

Duodenal ulcer in the early newborn period is rare and seldom suspected or diagnosed until hemorrhage or perforation occurs. Up to 1941 there were reports of only five newborn children, less than 14 days old, who were operated upon for a perforated gastric or duodenal ulcer; there was only one survival.

From a review of the literature, the authors believe that their patient is the fourth to have survived closure of a perforated duodenal ulcer in the early neonatal period, which they consider to be zero to 14 days of life. Their case report has additional interest since it is the first reported in which a premature infant survived closure of a perforated duodenal ulcer.

The first successful repair of a perforated gastric ulcer was reported in 1950 by Leger et al. Since then 11 more survivals of surgically treated gastric perforations have been reported in the newborn period, and the 12th case was recorded by Abramson and Folston in 1957.

So far as the authors know, perforation in the newborn infant has been uniformly fatal unless it has been closed surgically. Operation must be undertaken promptly and should be reduced to the minimum effective procedure.

CARL J. DEPRIZIO

UPPER GASTROINTESTINAL BLEEDING: Don C. Weir. Missouri Med. 56:265 (Mar.), 1959.

This is a discussion of the roentgen aspects of upper gastrointestinal bleeding. A consecutive group of 75 patients with massive upper gastrointestinal bleeding were carefully examined in the first 72 hours of hospitalization. It was found that duodenal ulcer was the source of the bleeding in 50 per cent, gastric ulcer in 17 per cent, esophageal varices in 11 per cent and hiatus hernia in 8 per cent.

The largest source of error was the superficial gastric ulcer. Blood clots in the stomach may simulate polypoid tumors. Double lesions caused errors and were present in nine patients. The presence of esophageal varices does not prove that this is the source of the bleeding for coexisting peptic ulcers were not uncommon.

In this series 29 per cent of the patients continued to bleed or rebleed. A control group of cases treated prior to 1950 when the roentgen examinations were not performed until two weeks after bleeding subsided were reviewed. In the latter group it was also found that 16 per cent rebled and 13 per cent continued to bleed. The author concludes that early radiological examination in the patient with massive upper gastrointestinal bleeding is of value because it establishes an early diagnosis, is not dangerous, and may reveal the coexistence of such lesions as peptic ulcer and esophageal varices, or peptic ulcer and hiatus hernia.

ARNOLD STANTON

INTESTINES

ELEVATION OF SERUM AMYLASE WITH POSTGASTRECTOMY JEJUNAL OBSTRUCTION AND PERFORATION: H. C. Ballon and P. N. Niloff. Canad. M. A. J. 80:339 (1 Mar.), 1959.

The diagnosis of an acute abdominal condition is always difficult and while the findings of an elevated serum amylase is of great value; the association of elevated serum amylase is also encountered with other acute abdominal conditions susceptible to surgical therapy. The authors, after a review of the literature, cite two cases of their own; postgastrectomy with jejunal obstruction and perforation. They point out that it is dangerous to assume that only pancreatitis (acute) can be responsible for elevated serum amylase values.

IRVIN DEUTSCH

EXPERIENCE WITH DIVERTICULITIS OVER A TEN-YEAR PERIOD: B. C. Payne and James Beatty. J. Michigan M. Soc. 58:377 (Mar.), 1959.

The authors present a critical analysis of 531 patients with diverticular disease of the colon seen over a ten-year period. Only 183 patients had symptoms relating to diverticulitis; 88 of them were treated medically, 58 required a variety of surgical procedures. It is if interest to note, that 11 patients of this latter group were operated upon under another diagnosis and not suspected to have diverticular disease.

The treatment of one complication—bleeding caused by diverticulitis—is discussed in detail. Conservative management as long as possible including large blood transfusions, is recommended.

In order to avoid diagnostic errors, especially acute appendicitis and rightsided tuboovarian disease, a preoperative barium colon enema is suggested.

This study again confirms the possibility of concurrent appearance of diverticula and sigmoid carcinoma. Consequently resection of the colon is indicated, whenever there is a question of the possible malignant nature of a lesion.

The clinical and radiological diagnosis of diverticulitis and diverticulosis are also discussed.

The fact is stressed, that one in two patients treated medically will have recurrences of diverticulitis, while the odds in surgically treated patients are one in five.

HANS J. JOSEPH

ACUTE APPENDICITIS: J. L. Ponka, H. L. Shields and D. M. Evans. J. Michigan M. Soc. 58:415 (Mar.), 1959.

Case histories of 451 patients with acute appendicitis, collected over a four-year period were reviewed by the authors. Complications were found in 91 cases, equal to 16.46 per cent. These complications consisted of peritonitis, abscess, wound infection, hernia, postoperative ileus, phlebothrombosis, pulmonary embolus, and subdiaphragmatic abscess. Different antibiotics and other treatments, i.e. Miller-Abbott tube, transfusions, etc., were employed to combat complications.

This high rate of complication can be avoided only by correct diagnosis and early surgery. The authors stress the fact, that antibiotics are not a cure for acute appendicitis, but are liable to lead to complications because of delay of operation.

HANS J. JOSEPH

BENIGN NEOPLASMS OF THE SMALL INTESTINE: George W. Lechner and Paul J. Connolly. J.A.M.A. 169:2003 (25 Apr.), 1959.

Although benign tumors of the intestine are admittedly uncommon, they can no longer be considered rare. In most series, benign tumors of the small intestine are found to be less frequent than malignant ones, averaging 30 to 45 per cent of the total. Seventy-five per cent of the benign tumors of the small intestine, in their relative orders of frequency, are adenomas, lipomas, myomas, polyps, fibromas, angiomas, or hemangiomas. The relative percentages of malignancy, as well as the incidence of all tumors, increase from the duodenum and jejunum to the ileum, being about 18, 25, and 57 per cent respectively. The majority of benign tumors are intraluminal and polypoid, and this accounts for the high incidence of intussusception with benign tumors. Intestinal obstruction is the most common single condition leading to the diagnosis, and is the presenting symptom in two-thirds of all cases, with three-fourths of these being due to intussusception. The next most common symptom is intestinal bleeding, usually as melena. About one-third of the reported cases have presented in this way, with massive bleeding occurring in about 11 per cent. Intussusception was a concomitant finding in half of the bleeding patients.

Definitive diagnosis is difficult preoperatively. In the most authoritative report, covering almost all the reported cases, the correct preoperative diagnosis was made in only 79 (7.8 per cent) of the 1,014 instances in which a tumor was found at operation. Careful small intestinal roentgen examination, preferably with thin barium, injected through an inlying Miller-Abbott tube, is the best method of diagnosis. A string test may help. Surgical excision is the only therapy.

SAMUEL M. GILBERT

GASTROINTESTINAL ALLERGY: Philip M. Gottlieb. Pennsylvania M. J. 62:551 (Apr.), 1959.

A comprehensive diagnostic approach will usually lead to a firm opinion. For this purpose, there are a number of diagnostic methods, one or more of which may be used in individual cases. The most commonly employed include elimination diets, provocative feeding trials, food diaries, and the administration of the suspected foods in disguised forms. Allergy skin tests with foods have a limited applicability, but are often of value. Roentgen and endoscopic studies are frequently helpful and are indispensable in differential diagnosis. The importance of a careful history cannot be overemphasized. A positive family history, the presence of blood eosinophilia, and the demonstration of eosinophils in the rectal mucus (in allergic diarrhea) add weight to the diagnosis.

Specific treatment consists primarily of elimination of the causative food, drug, or other offending allergen. Substitute foods are available for certain nutritional needs. When elimination of a food is not prac-

ticable oral (not parenteral) hyposensitization may be attempted, but is prolonged and often ineffective. The propeptan method, employing protein digests of the specific food according to a careful regimen, may often be successfully employed. Drug therapy is generally not too satisfactory. Antihistaminic preparations, antispasmodics and, when indicated, epinephrine may be tried. It is important to search for and treat possible predisposing factors.

JACOB A. RIESE

MECKEL'S DIVERTICULUM: X-RAY DIAGNOSIS: Alfred S. Berne. New England J. Med. 260:690 (2 Apr.), 1959.

The author reviews and re-emphasizes the radiological diagnostic signs of Meckel's diverticulum. He discusses the indirect signs of the complications which can occur in association with Meckel's such as: evidence of intestinal obstruction in the presence of free air or loculated air outside the intestinal tract secondary to perforation. He also discussed the direct x-ray signs of Meckel's on a flat plate of the abdomen. The lesion is frequently gas-filled. The detection of gas that does not conform to the usual bowel pattern may be a hint as to the presence of the diverticulum. On occasion an air fluid level may be seen within the diverticulum. The presence of opaque calculi which develop within these congenital diverticula is stressed. The author also stresses the use of contrast media in delineating diverticula. The value of both reflux from barium enema examinations and small bowel enema are stressed. He feels that the injection of barium or the administration of barium through a tube during a small intestinal enema is more satisfactory than a barium enema with reflux to demonstrate a Meckel's diverticulum. He re-emphasizes that careful examination of the small intestine increases the number of x-ray diagnoses of Meckel's diverticulum and he presents four cases diagnosed preoperatively by this method. The illustrations accompanying this article are superb.

RALPH D. EICHHORN

LIVER AND BILIARY TRACT

DETECTION OF INTREHEPATIC METASTASES BY BLIND NEEDLE LIVER BIOPSY: Albert D. Parets. Am. J. M. Sc. 237:335-340 (March), 1959.

The author reports 113 liver biopsies for detection of metastatic carcinoma. With the usual precautions, it was felt that no unwarranted risk was added. One patient with metastatic carcinoma developed bleeding and another peritonitis. Both patients recovered with proper treatment. The procedure can be used where the site of the primary carcinoma is unknown and it can also form the basis of decision for hepatic lobectomy or irradiation.

BERNARD FARFEL

IDENTIFICATION OF UNCOMMON LIVER LOBULATIONS: John H. Feist and Elliott C. Lasser. J.A.M.A. 169:1859 (18 April), 1959.

Four cases are reported to illustrate the frequent association of soft tissue masses in the right upper quadrant of the abdomen with symptoms suggesting pathology in this area. Liver lobulation can cause this type of confusion and the usual and unusual diagnostic examinations to identify the nature of the mass are listed. The technic using rose bengal with trace amounts of radioactive iodine and a scanning procedure is described. This technic may help eliminate the necessity for laparotomy.

BERNARD FARFEL

SERUM HEPATITIS FROM WHOLE BLOOD: INCIDENCE AND RELATION TO SOURCE OF BLOOD: Calvin M. Kunin. Am. J. M. Sc. 237:293-303 (March), 1959.

This article presents a study made to determine whether the increased incidence of serum hepatitis at a Veterans Administration hospital in Boston was due to inadequate screening methods used in a commercial source for procurement of blood or due to a population with an unusual number of carriers. The blood bank used appears to be at fault.

BERNARD FARFEL

HYPERBILIRUBINEMIA AND KERNICTERUS IN PREMATURE AND FULL-TERM BANTU NEWBORN INFANTS: M. H. Shnier and S. E. Levin. Brit. M. J. 5128:1004 (18 April), 1959.

Hsia et al showed a direct relationship between elevated serum bilirubin values and kernicterus. Bantu infants frequently show hyperbilirubinemia and kernicterus although Rh incompatibility is rare. The authors investigated 211 cases of neonatal jaundice seen in 5,000 deliveries. They excluded from their investigations 4 infants with Rh incompatibility. Fourteen of this series had kernicterus, 12 of these patients were prematures.

According to these researchers, kernicterus results from very high levels of indirect bilirubin in the serum, and this pigment is very toxic to the nervous tissues. Diarrhea with its attendant dehydration aggravates this condition. The study also indicates no relationship between serum bilirubin values and hemoglobin levels and suggests that hemolysis alone cannot be responsible for hyperbilirubinemia. Transfusion may result in "rebound phenomena" necessitating more exchange transfusions.

IRVIN DEUTSCH

COMMON DUCT STONE PRODUCING CHARCOT'S HEPATIC FEVER WITHOUT JAUNDICE: Frank M. Howard and William J. Martin. A.M.A. Arch. Int. Med. 103:565 (April), 1959.

Intermittent fever spells for a prolonged time, often for many months, may be caused by stones in the common duct. Chills and sweats, malaise, nausea and vomiting are frequently present during these attacks. Abdominal pain may be absent. The liver is usually enlarged and tender. Previous history of gallbladder disease or gallbladder operation, presence of gallstones, nonfilling of gallbladder and bile ducts after oral or intravenous dye and abnormal liver function tests, especially elevated serum bilirubin and alkaline phosphatase and bromsulfaphthalein retention, may point toward the correct diagnosis. On the other hand fever and chills may be entirely absent in cholodocholithiasis. Usually an exploratory laparotomy has to be made to verify the diagnosis.

H. B. EISENSTADT

POLYCYSTIC DISEASE OF THE LIVER: Paul E. Geiger. Ohio M. J. 55:668 (May), 1959.

Polycystic disease of the liver is a rather rare congenital condition and is often associated with polycystic disease of the kidneys. The writer adds another case to the literature in which as usual the diagnosis was made by surgical exploration including liver biopsy.

WALTER CANE

SPONTANEOUS INTERNAL BILIARY FISTULA: Norman R. Wall and Grafton A. Smith. Missouri Med. 56:523 (May), 1959.

Biliary fistula is a connection between the biliary tract and some portion of the intestinal tract; very rarely is the liver additionally involved. The commonest types are cholecystoduodenal, cholecystocolic, and choledochoduodenal. The etiology is gallstones 90 per cent, perforating ulcer 6 per cent, and carcinoma 4 per cent. The incidence in which it is found at autopsy with gallstones varies from 0.11 to 0.39 per cent;

yet in gallbladder operations, the incidence has been reported from 3.5 to 7 per cent.

At times, the condition is almost symptomless and discovered accidentally at x-ray examination; on the other hand, x-ray examination may fail to disclose the condition. The symptoms are usually upper abdominal pain, tenderness, muscle guarding, and mass in various combinations which would ordinarily lead to a diagnosis of acute cholecystitis, gallstone colic, or complicated peptic ulcer.

Diagnosis essentially depends on x-ray examination—the entrance of air or barium into the biliary system. It is necesary to differentiate a relaxed sphincter of Oddi, in which barium is seen in the distal portion of the common duct, encountered when a large stone has passed through, also in pancreatitis and temporarily after cholecystectomy. In fistula, the mucous membrane shows irregularity of the folds.

Infection – abscess formation, subdiaphragmatic abscess, and ascending biliary infection; gallstone ileus or internal hemorrhage may occur.

Some recommend delay in operation if there are no symptoms, but surgical treatment is more difficult if symptoms are present. The death rate is most frequently related to infection or hepatic insufficiency. Surgical treatment requires great skill and judgment. Ascending cholangitis and liver failure may improve only by a direct attack and correction of the abnormal fistula and any related biliary tract disease, but if localized pus is encountered at the time of celiotomy, simple drainage is preferable to an extended vigorous dissection. If dissection compromises the colon in cases of active infection, a double-barreled colostomy or some other type of procedure is employed and the patient operated on later for the fistula. The exploration at the time of operation is extensive. In suspected pancreatic involvement, a palpable pancreatic duct is suspicious of a neoplasm. A fine needle inserted through the head of the pancreas grates against a stone and differentiates from neoplasm.

Operative cholangiography is performed through the fundus of the gallbladder or an accessible radical, thus outlining the tract. Exploration of the biliary tract may discover a stone in the ampulla of Vater, especially in the duodenal fistula type. Stricture of the bile duct is usually not severe, and the duct can usually be closed over a T-tube. In case of major stricture or severance of the common duct, the surgeon naturally prefers an end-to-end anastomosis and a proximal T-tube; if obstruction recurs at a later date, the duodenum or jejunum can be used as a site of anastomosis. If cholangitis occurs, the jejunal type of anastomosis is used—the Roux-en-Y.

Peptic ulcer fistula with stone is managed in a number of ways. Drainage of the common duct or gallbladder may be employed if the patient is jaundiced. The ulcer may then heal and the fistula close, but a second operation may be necessary for the ulcer. If the patient's condition warrants, both operations may be performed as one; with various modifications as indicated, as in the case of gallstone disease, stricture, etc.

The preoperative preparation includes the use of antibiotics and disinfection of the colon. The authors operated on seven patients with two deaths.

SAMUEL L. IMMERMAN

DRUG-INDUCED JAUNDICE: Charles H. Brown and William F. Gebhart. Mississippi Valley M. J. 81:156 (May), 1959.

The wide and expanding use of drugs in modern therapy dictates that a drug reaction be considered when jaundice is a presenting finding.

Drugs are causing jaundice by two different mechanisms: an allergic cholangitis bearing no relation to dosage and resulting in an obstructive jaundice or by a toxic effect on hepatic cells, causing varying degrees of necrosis in some proportion to the amount of drug administered.

By either mechanism the incidence is very low considering the extensive use or exposure of these common drugs such as chlorpromazine, Nilevar, Pas and methyltesterone, all four being given as examples of drugs causing allergic cholangitis. Gold, urethane, atabrine, phenylbutazone, antibiotics and isoniazid or iproniazid are given as hepatocellular toxins when they behave as such.

The rise in incidence of postnecrotic cirrhosis may be possibly due to drugs in some instances although the condition probably has diverse etiologies.

A. M. SUSINNO

BOOK REVIEWS FOR GASTROENTEROLOGISTS

CONSTRUCTION OF RESEARCH FILMS: D. H. Densham, Published for and on behalf of the Advisory Group for Aeronautical Research and Development North Atlantic Treaty Organization. 104 pages, illustrated. Pergamon Press, Inc., New York, N. Y., 1959. Price $4.50.

This book deals with the camera, settings, taking and developing scientific films for instruction and research.

Industrial concerns, schools and universities who do their own cinemography will find it of great value.

MENTAL RETARDATION: ITS CARE, TREATMENT AND PHYSIOLOGICAL BASE: Hans Mautner, M.D., Pineland Hospital and Training Center, Pownal, Maine. 280 pages. Pergamon Press, Inc., New York, N. Y., 1959. Price $5.00.

Psychiatrists, social workers and others who work with the mentally retarded, will find invaluable data in this book.

Interesting and instructive discussion regarding the availability of tranquilizers, should be of interest to all physicians.

Adequate references, name and cross index complete the volume.

BLEEDING ESOPHAGEAL VARICES—PORTAL HYPERTENSION: Hirsch Robert Liebowitz, B.S., M.D., Assistant Professor of Clinical Medicine, New York University College of Medicine and Chief of the Gastrointestinal Clinic, (N.Y.U.) Bellevue Hospital, Consulting Gastroenterologist, Institute of Physical Medicine and Rehabilitation of Physical Medicine, New York University Bellevue Medical Center. Section on Surgical Treatment in Collaboration with Louis M. Rousselot, M.D., M.S. (Surg.), Med.Sc.D. (Surg.); F.A.C.S., Director of Surgery, St. Vincent's Hospital, New York, N. Y., Professor of Clinical Surgery, New York University College of Medicine; with a foreword by Allen O. Whipple, M.D., F.A.C.S., Emeritus Valentine Mott, Professor of Surgery, College of Physicians and Surgeons, Columbia University. 980 pages, illustrated. Charles C Thomas, Springfield, Ill., 1959. Price $24.50.

A monograph dealing with a special phase, "Bleeding Esophageal Varices and Portal Hypertension", is a work of a lifetime. Not everyone would undertake the enormous task, time and energy that Dr. Liebowitz devoted to this most instructive book.

The illustrations, references and index add to the value of the text and physicians should not hesitate to add this volume to their library.

LONG-TERM ILLNESS. MANAGEMENT OF THE CHRONICALLY ILL PATIENT: Edited by Michael G. Wohl, M.D., F.A.C.P., Former Clinical Professor of Medicine (Endocrinology), Philadelphia General Hospital and Temple University School of Medicine; Chief of Nutrition Clinic, Philadelphia General Hospital; Consultant Physician in Medicine, Albert Einstein Medical Center; Attending Physician, Home for the Jewish Aged, with the collaboration of 79 contributing authorities. 748 pages, illustrated. W. B. Saunders Company, Philadelphia, Pa., 1959. Price $17.00.

It was a herculean task to edit this excellent volume and to correlate the various diseases, so that the general practitioner and the specialist may benefit by the sage advice and outlined therapy in a given case. Many of the contributors are known to the reviewer for their clinical acuity and teaching experience in the various medical schools.

The two column arrangement makes reading a pleasure and the tables and illustrations add to the value of the text. Dr. Wohl, his colleagues, as well as the publisher, are to be commended for their cooperation in bringing out this worthwhile volume. It is highly recommended.

CURRENT THERAPY—1959: Edited by Howard C. Conn, M.D., with 12 Consulting Editors and an array of Internists and Surgeons. 781 pages. W. B. Saunders Co., Philadelphia, Pa., 1959. Price $12.00.

In addition to the text by the distinguished collaborators, the physician will find useful data on burns, disturbances due to heat, acute barbiturate poisoning, poisonous substances in 48 household items and much other useful information.

In the appendices are: a roster of drugs, table of pediatric dosages, metric and apothecary systems, preparation of percentage solutions followed by an extensive index.

The editor and the publisher are to be highly commended for this useful, well printed bound volume. It is recommended for the library of the physician.

THE MODERN FAMILY HEALTH GUIDE. A NEW MAJOR HOME-REFERENCE VOLUME OF AUTHORITATIVE MEDICAL ADVICE AND GUIDANCE BY 27 NOTED DOCTORS AND SPECIALISTS: Edited by Morris Fishbein, M.D., Formerly Editor, Journal of the American Medical Association, Editor, Excerpta Medica, Medical Editor, Britannica Book of the Year. 1001 pages. Doubleday and Company, Inc., Garden City, N. Y., 1959. Price $7.50.

Although written for the laity, the general practitioner will find useful information in it, or he may want to clarify some points when discussing the patient's condition. It specifically cautions the laity not to attempt to diagnose or medicate themselves, members of their family or neighbors.

In addition to the various diseases, there is an excellent encyclopedia of medical terms with simplified definitions and last but not least, a cross reference to easily find what one is looking for.

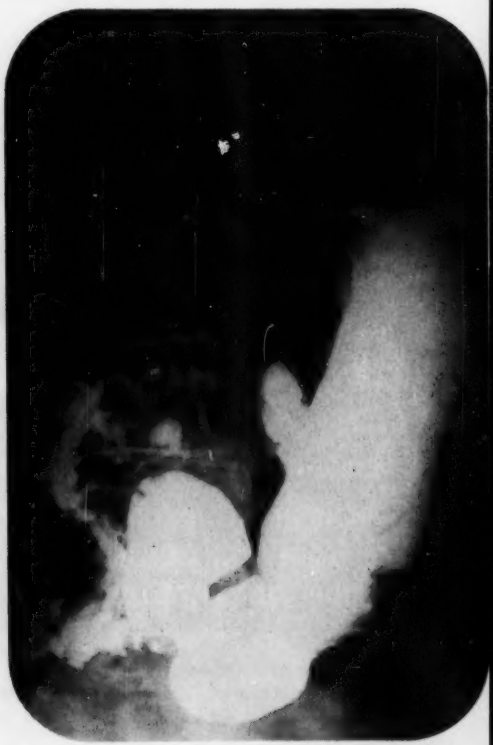
Rural physicians will find it to their advantage to have a copy in their office or to recommend it to their patients.

EFFECTIVENESS OF "MUREL"-S. A. IN SPASM VISUALLY CONFIRMED

55 year old male with symptoms of partial obstruction of the stomach; nausea and vomiting.

March 1st, 1960: Large dilated stomach with incomplete pyloric obstruction. Etiology undetermined.

Patient placed on "Murel"-S.A.—2 tablets b.i.d. for one week—plus bland diet. No other medication.



March 10th, 1960: Stomach of normal size and tone. Large ulcer crater now visualized in the region of previously noted pyloric spasm and incomplete filling.

Medical Records of Ayerst Laboratories

in G.I., G.U. and Biliary SPASM

"Murel"-S.A.

Sustained Action Tablets

prompt, continuous and prolonged antispasmodic action for 6 to 9 hours with a single tablet

"MUREL" Advantages[1-4]

- Exceptionally effective clinically because three-way mechanism of action in one molecule (anticholinergic, musculotropic, ganglion-blocking) exerts synergistic spasmolytic effect
- Complementary action permits significantly low dosage and reduces reaction potential of any one mechanism
- Remarkably free from drug-induced complications such as mouth dryness, visual disturbances, urinary retention

Suggested Average Dosage: 40 to 80 mg. daily, depending on condition and severity. The higher range of dosage is usually required in spasm of the genitourinary and biliary tracts. One "Murel"-S.A. Sustained Action Tablet morning and evening. *When anxiety and tension are present,* "Murel" with Phenobarb-S.A. is suggested.

Available as: No. 315—"Murel"-S.A., 40 mg. Valethamate bromide; and No. 319—"Murel" with Phenobarb-S.A., with ½ gr. phenobarbital, present as the sodium salt. Both in bottles of 100 and 1,000.

Also available: "Murel" Tablets No. 314—10 mg. Valethamate bromide; "Murel" with Phenobarbital Tablets No. 318—10 mg. Valethamate bromide and ¼ gr. phenobarbital.

"Murel" Injectable No. 405—10 mg. Valethamate bromide per cc.

Precautions: As with other antispasmodic agents, caution should be exercised in patients with prostatic hypertrophy, glaucoma, and in the presence of cardiac arrhythmias.

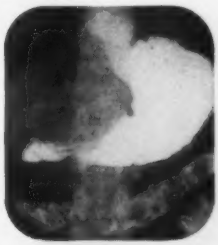
References available on request.

AYERST LABORATORIES
New York 16, N.Y. • Montreal, Canada

for acute, severe episodes
"MUREL" Injectable

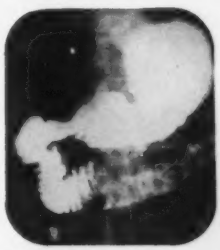
Female patient, age 55, complaining of nausea and epigastric discomfort after meals.

Diagnosis: Hiatus hernia and gastric ulcer.



1 hour after barium administration: Retention of barium due to spasticity of the gastric outlet, and incomplete visualization of the pylorus, duodenum and duodenal sweep. (Some barium has entered the small bowel.)

20 minutes after administration of "Murel" 2 cc. I.V.: Barium entering duodenum and duodenal sweep as spasticity is relieved.



10 minutes later: Good filling of the gastric outlet as well as of the duodenal sweep.

Medical Records of Ayerst Laboratories 6027

rapid, reliable

relief *of* gastritis

and related disorders such as

indigestion • heartburn • spastic colon

nausea and vomiting • esophagitis

irritable bowel • dyspepsia

OXAINE*

containing a gastric mucosal anesthetic

OXAINE relieves pain, breaking the pain-food-pain cycle common to gastritis. With pain relief, patients can often enjoy an increased variety and volume of food; consequently their psychological outlook is brightened.

OXAINE is equally effective in many other disorders related to gastritis. You will find it especially useful in gastric disorders not totally manageable by diet, antacids, and anticholinergics.

"*Ninety-six per cent of the* [*92*] *patients obtained complete relief of substernal pain or upper abdominal distress lasting two to six hours after each dose.*"†

Detailed Information on

OXAINE

Oxethazaine in Alumina Gel, Wyeth

OXAINE combines the antacid and demulcent properties of AMPHOJEL® (aluminum hydroxide gel) with the pain-relieving action of *oxethazaine*, a new, very effective topical anesthetic. Gastroscopic observations reveal that AMPHOJEL, especially when swallowed undiluted, is an adherent vehicle. Oxethazaine exerts a prolonged topical anesthetic action on the mucosa.

INDICATIONS

Gastritis: In chronic gastritis, OXAINE provides relief of substernal pain and upper abdominal distress and permits patients a pronounced increase in the volume and variety of food intake. Medical management of gastritis should include physical rest, small meals of bland foods, and adequate fluid intake. In acute phases, fasting, bed rest, and gastric suction may be indicated. Initial feeding should consist of clear liquids rather than the fatty foods often prescribed for peptic-ulcer patients.

Gastritis occurs more frequently than peptic ulcer; both may occur concurrently, however. The pain pattern of chronic gastritis is usually the reverse of that typical of peptic ulcer. Food usually provides relief of ulcer; the distress of gastritis occurs on ingestion of food. Initially, the pain is intermittent; later, it may become constant and intractable. One of the earliest symptoms is upper abdominal pain following the major meal. Eventually, the same pain recurs after almost *every* meal; then belching after the major meal becomes distressing. The upper abdominal discomfort, belching, and restlessness increase in frequency and severity. Then nausea, vomiting, and general weakness become complicating factors. Constipation, prolonged fluid deficit and intolerance of fresh fruits and vegetables may be associated. Fear of cancer may be disabling. Physical examination often shows only tenderness on light percussion or palpation of the upper abdomen. Abdominal distention may be noticeable. Gastric analysis may show hyper- or hypochlorhydria.

Esophagitis: OXAINE therapy relieves discomfort and lessens the frequency with which esophageal dilatation is required. Patients should sleep with the back and head elevated to minimize reflux of gastric contents into the lower end of the esophagus.

Irritable colon syndrome: In patients with this common functional disorder of the gastrointestinal tract, OXAINE diminishes the sensitivity of the gastrocolic reflex. Among a variety of vague complaints are discomfort in the left lower abdomen and sometimes crampy pain and nausea. The urge to defecate often follows ingestion of food. A low residue, bland diet is often indicated; also attention to psychosomatic aspects.

DOSAGE AND ADMINISTRATION. The recommended adult dose is one or two teaspoonfuls four times daily, 15 minutes before meals and at bedtime. Do not exceed recommended dosage.

PRECAUTIONS. Adequate diagnostic studies are recommended. The possibility of gastrointestinal carcinoma should be considered in patients with protracted or recurrent indigestion. Constipation, which may be aggravated by therapeutic doses of OXAINE, should be prevented by adequate fluid intake and dietary roughage or mineral oil preparation (such as PETROGALAR®).

If the dose of OXAINE exceeds 12 teaspoonfuls a day, some patients may experience dizziness, faintness, or drowsiness. Two cases of glossitis of the hypersensitivity type have been reported in extensive clinical studies. One observed case of skin eruption was relieved by discontinuation of medication.

SAFETY: A wide margin of safety exists between the effective dose and oral toxic dose of oxethazaine in aluminum hydroxide gel. In mice, the oral LD_{50} of oxethazaine when suspended in aluminum hydroxide gel is 1012 mg. of base per kg. The effective dose of OXAINE, one or two teaspoonfuls, contains 10 or 20 mg. of oxethazaine respectively; this is only 0.2 or 0.4 mg. per kg. of body weight for a 50 kg. human being. In human beings, toxic effects have not been observed on continued ingestion of recommended therapeutic doses.

For further information on prescribing and administering OXAINE *see descriptive literature, available on request.*

†Deutsch, E., and Christian, H.J.: Chronic gastritis; histological criteria for management and medical treatment with a mucosal anesthetic in aluminum hydroxide, J. Am. Med. Assoc. *169*: 2012 (April 25) 1959.

Wyeth Laboratories Philadelphia 1, Pa.

A Century of Service to Medicine

*Trademark

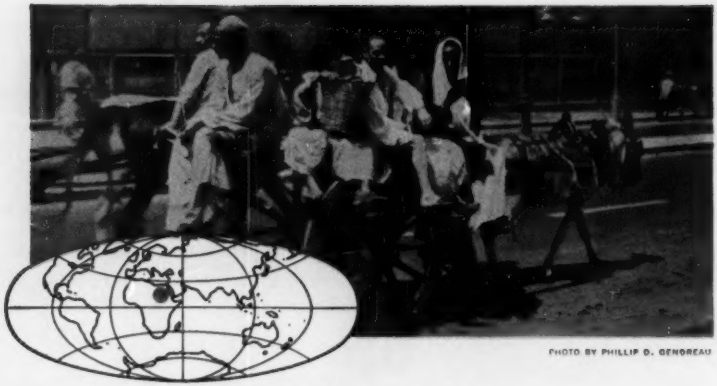


PHOTO BY PHILLIP D. GENDREAU

world-wide evidence favors Furoxone for bacterial diarrheas

In Egypt, Furoxone® effective against shigella strains now resistant to other antimicrobials

Cairo investigators administered FUROXONE for one week to 37 patients with shigellosis, reported all 37 clinically cured, 35 free of shigella prior to completion of FUROXONE therapy.

FUROXONE was tested in light of evidence that shigella strains resistant to sulfonamides, tetracyclines and chloramphenicol now exist. Observations: "All shigella isolated were sensitive in vitro to [FUROXONE]". Clinically, FUROXONE "significantly reduces the duration and severity of the diarrhea and effects bacteriological cure .... The absence of toxic or side effects gives [FUROXONE] an advantage not possessed by the other drugs in current use."

Musgrave, M. E., and Arm, H. G.: Antibiotic Med. & Clin. Therapy 7:17 (Jan.) 1960.

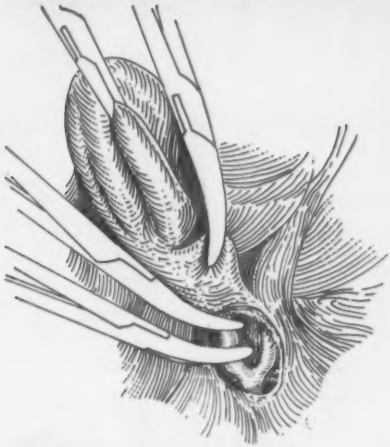
FUROXONE LIQUID: a suspension containing FUROXONE 50 mg. per 15 cc., with kaolin and pectin, bottles of 240 cc. **FUROXONE TABLETS:** 100 mg., scored, bottles of 20 and 100. **DOSAGE:** should provide (in 4 divided doses) 400 mg. daily for adults, 5 mg./Kg. daily for children.

FUROXONE

THE NITROFURANS—a *unique* class of antimicrobials
EATON LABORATORIES, NORWICH, NEW YORK

AN AMES CLINIQUICK®

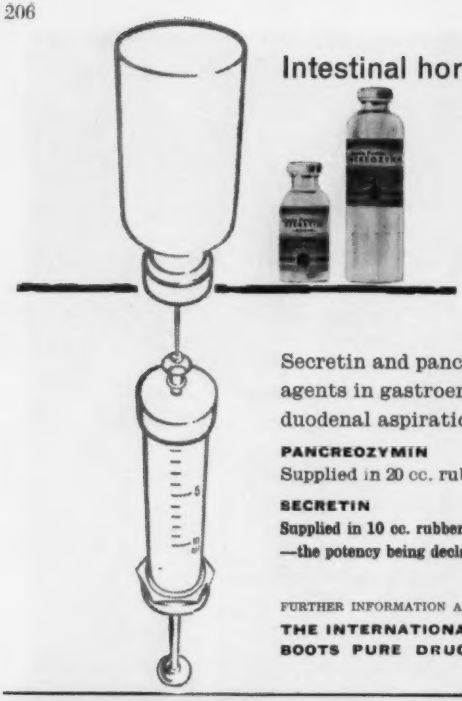
CLINICAL BRIEFS FOR MODERN PRACTICE



HOW MAY A PATIENT BE REASSURED THAT REMOVAL OF HIS GALLBLADDER WILL NOT SERIOUSLY IMPAIR HIS DIGESTIVE ABILITY?

He may be told that, among animals of similar dietary habits and digestive processes, some have a gallbladder and some do not. Among the herbivores, the cow and sheep have one, the deer and horse do not; among the omnivores, the mouse has one but the rat does not.

Source: **Farris, J. M., and Smith, G. K.: M. Clin. North America *43*:1133 (July) 1959.**



Intestinal hormones in pure and stable form

Secretin and Pancreozymin

Secretin and pancreozymin are of proved value as diagnostic agents in gastroenterology and may be used confidently in the duodenal aspiration test and the serum enzyme test.

PANCREOZYMIN
Supplied in 20 cc. rubber-capped vials each containing 100 units.

SECRETIN
Supplied in 10 cc. rubber-capped vials each containing from 50-100 units —the potency being declared on each vial following biological assay.

FURTHER INFORMATION AND SUPPLIES FROM:
THE INTERNATIONAL DIVISION
BOOTS PURE DRUG CO. LTD. NOTTINGHAM ENGLAND

Boots

ROMACH
FOR PEPTIC ULCER

Succeeds in 90% of Cases

Many published articles have established the outstanding value of Romach tablets for prompt relief and ultimate healing of gastric and duodenal ulcers.

A study in England reported a satisfactory response to Romach in 90% of cases.

An American article[2] reported relief of pain without analgesics in 92% cases, weight gains averaging 7.9 lb. in 93% cases, control of occult blood in stools in 100% cases, and ultimate roentgenographic healing of the ulcers in 81% cases.

The recommended dosage of Romach is 2 tablets in tepid water immediately after meals.

ROR CHEMICAL CO. • 2268 First Ave. • New York 35, N. Y.

AJG—8

ROR CHEMICAL CO., 2268 First Ave., New York 35, N. Y.

Please send me without obligation professional sample, complete formula and literature on Romach tablets.

.....M.D.

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City.....Zone.....State.....

1. *British Medical Journal* 2:827, 1955
2. *American Journal of Gastroenterology* 28:439, 1957

after milk and rest, why Donnalate?

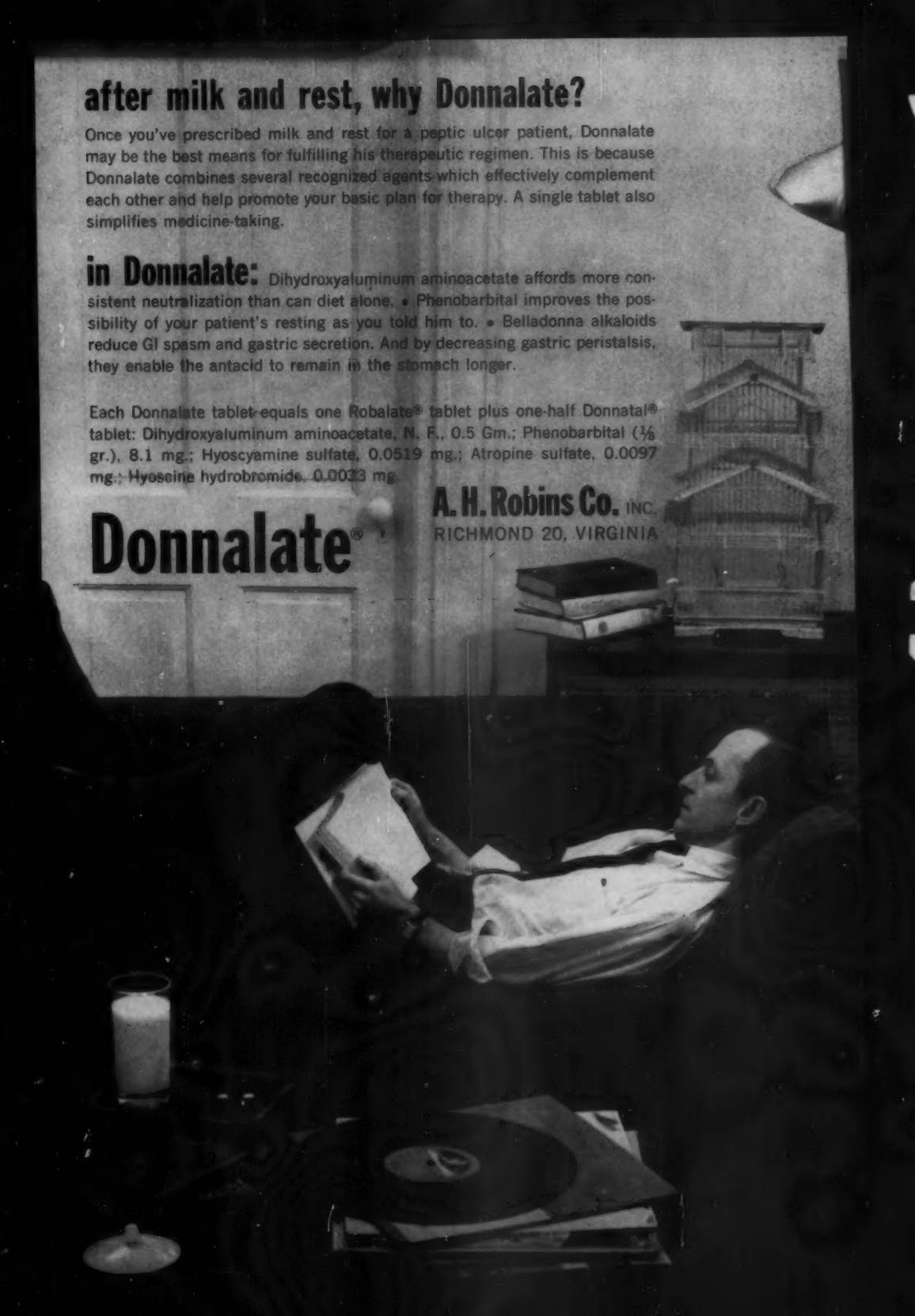
Once you've prescribed milk and rest for a peptic ulcer patient, Donnalate may be the best means for fulfilling his therapeutic regimen. This is because Donnalate combines several recognized agents which effectively complement each other and help promote your basic plan for therapy. A single tablet also simplifies medicine-taking.

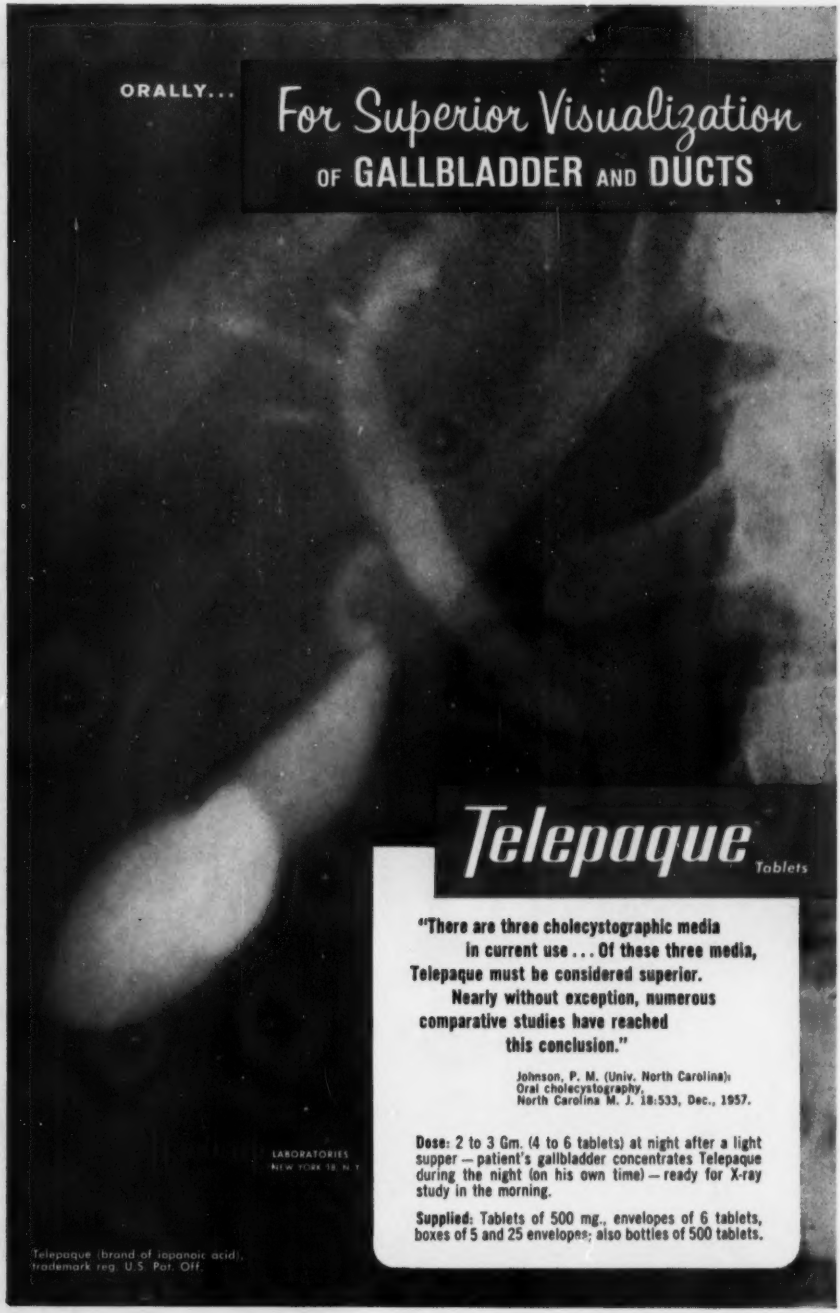
in Donnalate: Dihydroxyaluminum aminoacetate affords more consistent neutralization than can diet alone. • Phenobarbital improves the possibility of your patient's resting as you told him to. • Belladonna alkaloids reduce GI spasm and gastric secretion. And by decreasing gastric peristalsis, they enable the antacid to remain in the stomach longer.

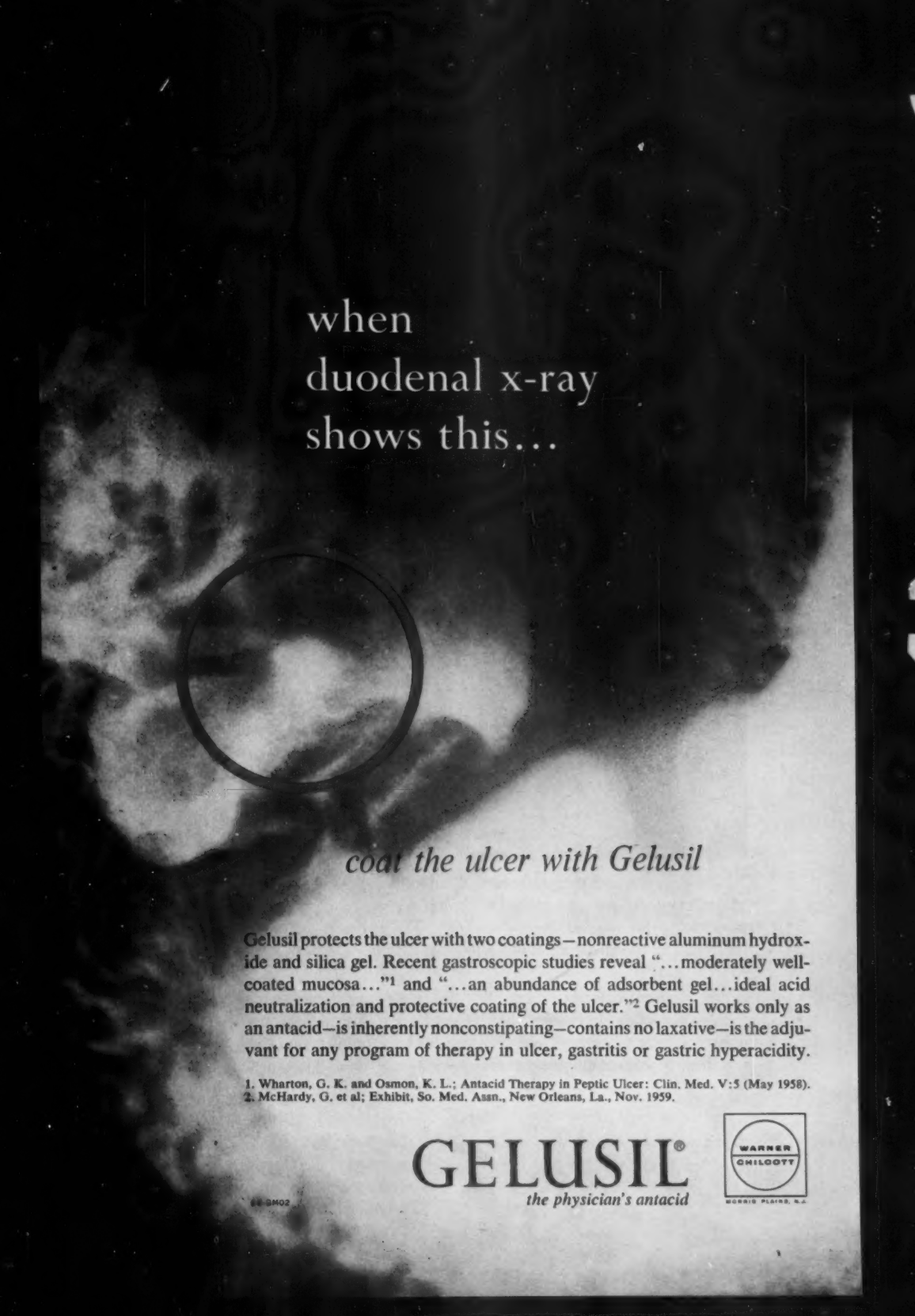
Each Donnalate tablet equals one Robalate® tablet plus one-half Donnatal® tablet: Dihydroxyaluminum aminoacetate, N. F., 0.5 Gm.; Phenobarbital (1/8 gr.), 8.1 mg.; Hyoscyamine sulfate, 0.0519 mg.; Atropine sulfate, 0.0097 mg.; Hyoscine hydrobromide, 0.0033 mg.

Donnalate®

A. H. Robins Co. INC.
RICHMOND 20, VIRGINIA




ORALLY...
For Superior Visualization
OF GALLBLADDER AND DUCTS
Telepaque Tablets
"There are three cholecystographic media in current use ... Of these three media, Telepaque must be considered superior. Nearly without exception, numerous comparative studies have reached this conclusion."
Johnson, P. M. (Univ. North Carolina): Oral cholecystography, North Carolina M. J. 18:533, Dec., 1957.
Dose: 2 to 3 Gm. (4 to 6 tablets) at night after a light supper — patient's gallbladder concentrates Telepaque during the night (on his own time) — ready for X-ray study in the morning.
Supplied: Tablets of 500 mg., envelopes of 6 tablets, boxes of 5 and 25 envelopes; also bottles of 500 tablets.
LABORATORIES
NEW YORK 18, N.Y.
Telepaque (brand of iopanoic acid), trademark reg. U.S. Pat. Off.


when
duodenal x-ray
shows this...
coat the ulcer with Gelusil
Gelusil protects the ulcer with two coatings—nonreactive aluminum hydroxide and silica gel. Recent gastroscopic studies reveal "...moderately well-coated mucosa..."1 and "...an abundance of adsorbent gel...ideal acid neutralization and protective coating of the ulcer."2 Gelusil works only as an antacid—is inherently nonconstipating—contains no laxative—is the adjuvant for any program of therapy in ulcer, gastritis or gastric hyperacidity.
1. Wharton, G. K. and Osmon, K. L.; Antacid Therapy in Peptic Ulcer: Clin. Med. V:5 (May 1958).
2. McHardy, G. et al; Exhibit, So. Med. Assn., New Orleans, La., Nov. 1959.
GELUSIL®
the physician's antacid
WARNER CHILCOTT
MORRIS PLAINS, N.J.
66-3M02

Diagnostic Quandaries

Colitis? Gall Bladder Disease?
Chronic Appendicitis?
Rheumatoid Arthritis? Regional Enteritis?

A DISEASE that is frequently overlooked in solving diagnostic quandaries is amebiasis. Its symptoms are varied and contradictory, and diagnosis is extremely difficult. In one study, 56% of the cases would have been overlooked if the routine three stool specimens had been relied on.[1]

Another study found 96% of a group of 150 patients with rheumatoid arthritis were infected by *E. histolytica*. In 15 of these subjects, nine stool specimens were required to establish the diagnosis.[2]

Webster discovered amebic infection in 147 cases with prior diagnoses of spastic colon, psychoneurosis, gall bladder disease, nervous indigestion, chronic appendicitis, and other diseases. Duration of symptoms varied from one week to over 30 years. In some cases, it took as many as six stool specimens to establish the diagnosis of amebiasis.[3]

Now treatment with Glarubin provides a means of differential diagnosis in suspected cases of amebiasis. Glarubin, a crystalline glycoside obtained from the fruit of *Simarouba glauca*, is a safe, effective amebicide. It contains no arsenic, bismuth, or iodine. Its virtual freedom from toxicity makes it practical to treat suspected cases without undertaking difficult, and frequently undependable, stool analyses. Marked improvement following administration of Glarubin indicates pathologically significant amebic infection.

Glarubin is administered orally in tablet form and does not require strict medical supervision or hospitalization. Extensive clinical trials prove it highly effective in intestinal amebiasis.

Glarubin*

TABLETS

specific for intestinal amebiasis

Supplied in bottles of 40 tablets, each tablet containing 50 mg. of glaucarubin.

Write for descriptive literature, bibliography, and dosage schedules.

1. Cook, J.E., Briggs, G.W., and Hindley, F.W.: Chronic Amebiasis and the Need for a Diagnostic Profile, Am. Pract. and Dig. of Treat. *6*:1821 (Dec., 1955).

2. Rinehart, R.E., and Marcus, H.: Incidence of Amebiasis in Healthy Individuals, Clinic Patients and Those with Rheumatoid Arthritis, Northwest Med., *54*:708 (July, 1955).

3. Webster, B.H.: Amebiasis, a Disease of Multiple Manifestations, Am. Pract. and Dig. of Treat. *9*:897 (June, 1958).

*U.S. Pat. No. 2,864,745

THE S.E. MASSENGILL COMPANY

BRISTOL, TENNESSEE

NEW YORK • KANSAS CITY • SAN FRANCISCO

Cremomycin® provides rapid relief of virtually all diarrheas

NEOMYCIN—rapidly bactericidal against most intestinal pathogens, but relatively ineffective against certain diarrhea-causing organisms.

SULFASUXIDINE® (succinylsulfathiazole)—an ideal adjunct to neomycin because it is highly effective against Clostridia and certain other neomycin-resistant organisms.

KAOLIN AND PECTIN—coat and soothe the inflamed mucosa, adsorb toxins, help reduce intestinal hypermotility, help provide rapid symptomatic relief.

For additional information, write Professional Services, Merck Sharp & Dohme, West Point, Pa.

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